NASA Contractor Report 3922(26)

USSR Space Life Sciences Digest

Issue 22

CONTRACT NASW-4292
AUGUST 1989

NASA

NASA Contractor Report 3922(26)

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Prepared for
NASA Office of Space Science and Applications
under Contract NASW-4292

National Aeronautics and
Space Administration
Office of Management
Scientific and Technical
Information Division

1989

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USSR Space Life Sciences Digest: Issue 22 Reader Feedback Form

To our readers: We are working in a large number of highly technical, specialized areas for which adequate Russian-English glossaries have yet to be compiled. We ask your help in improving the accuracy and specificity or our English terminology. Please fill out the form below whenever you encounter an incomprehensible, incongruous, awkward or otherwise inappropriate term. While we solicit all suggestions for improved renderings, the statement that a term is inappropriate provides us with useful information, even when no better alternative can be suggested. A copy of this form will appear in all future issues of the Digest. Thank you for your help.

Abstract Number	Incorrect or inappropriate term	Suggested rendering

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FROM THE EDITORS

This is Issue 22 of the USSR Space Life Sciences Digest. This is a special double issue covering two numbers (22(6) and 23(1) of *Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.* The current issue contains not only an expanded Table of Contents, listing all abstract titles, but also, for the first time, a key word index, located at the back of the issue. Of particular interest is a special feature providing a translation of an interview with two Mir cosmonauts.

The following 25 abstracts present or discuss Soviet space flight data: Cardiovascular and Respiratory Systems: P982; Developmental Biology P1004 -10018, Gravitational Biology P1000, Life Support Systems P989, Musculoskeletal System P 992, P1035, Psychology P987, Radiobiology P990, Reproductive System P983, Space Biology and Medicine P991 and P986.

It may be of interest to readers to learn that Joint Publications Research Service (JPRS) is no longer translating *Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.*cover to cover, and has not been doing so for approximately the last 18 months. To our knowledge, this Digest is now the only regular source of detailed information on the contents of this Soviet journal.

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ADAPTATION

PAPERS:

P1028(22/89)* Krivoshchekov SG, Neshumova TV, Razumenko AA, Tataurov YuA.
Energy metabolism and physical work efficiency in humans adapting to high altitude conditions.
Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.
23(1): 62-66; 1989.
[6 references; 1 in English]

Metabolism, Musculoskeletal System, Work Efficiency, Exercise, Cardiovascular and Respiratory Systems, Endocrinology, Enzymology
Humans, Males, Athletes
Adaptation, High Altitude

Abstract: The goals of this work involved: determination of how the efficiency of physical exercise changes in humans during 1 month's exposure to high altitude conditions and 1 week after return to sea level; evaluation of parameters of energy metabolism and cardiovascular function during the same period; and identification of how metabolic changes support stability of work capacity at various stages of adaptation. Subjects were 14 highly qualified mountain climbers aged 27-35. The study was conducted during the summer in the mountains of Pampir. Over the course of a 30-day period the subjects engaged in a great deal of strenuous exercise, climbing from the base camp (3000 m) to various heights (4000-5000 m). Each subject was studied in 5 measurement sessions: I - baseline (at sea level); II, III, IV - respectively on days 2-3, 14-16, and 27-29 of their time in the mountains; V - days 5-7 after return to sea level. Measurements II, III, and IV were made at an altitude of 1000 m. Nonathletes performing the same tests at sea level were used for controls. During measurement sessions, subjects underwent a 5-minute exercise session (2 W/kg) on a bicycle ergometer. Cardiorespiratory function was measured before exercise, throughout exercise, and during a 12-minute recovery period. Heart rate, blood pressure, respiratory minute volume, O_2 pressure in exhaled air, and temperature of the femur were measured. Oxygen pulse (seemingly stroke volume of oxygen), oxygen consumption, and pulse pressure were also measured. Efficiency was computed as the ratio of work performed on the ergometer to energy expended above resting level, computed on the basis of oxygen consumption considering caloric equivalents. Cardiac cost of work was computed as number of heartbeats during work and recovery above the resting level. Venous blood was taken at 8-9 a.m. on an empty stomach and centrifuged at 0° C; a hemolysate of erythrocytes was frozen and stored. Concentrations of insulin, hydrocortisone, and growth hormone were measured in serum using radioimmune assay. Activity of key enzymes was determined in the erythrocyte hemolysate, using glucose and glucoso-6-phosphate for the substrate.

During the initial period of adaptation, exercise induced a greater increase in oxygen consumption than that noted at baseline or later. This increase was observed both during and after exercise. Computation of energy cost and efficiency showed that during the first 14 days, efficiency was decremented by 20% compared to baseline. After 3 days of adaptation, there was some increase in efficiency, but it did not reach baseline levels. During readaptation, efficiency was a mean of 30% above baseline. The cardiac cost of exercise did not change during the first few days of high altitude adaptation, but subsequently decreased. By the end of a month's adaptation, pulse pressure and systolic and diastolic blood pressure were slightly below comparable baseline levels during exercise and the first minute of recovery. By the end of the adaptation period, oxygen pulse increased more in response to exercise than it did during the baseline and readaptation periods. Skin temperature of the femur increased slightly during the exercise test toward the end of the adaptation period. During adaptation, concentration of hydrocortisone increased by a factor of 2.5, and insulin decreased by a factor of 2.5-3. During

readaptation hydrocortisone returned to normal, but insulin continued to be depressed. No changes were noted in activity of hexokinase or phosphofructokinase during adaptation, but during readaptation their activity increased. Increased somatotropic function of the hypophysis is evidently associated with the fact that exercise is a powerful stimulant of the hypothalamus-hypophysis system with regard to growth hormone.

The authors conclude that the combined effects of exercise and high altitude hypoxia lead to a number of complex, adaptive physiological and biochemical restructurings, Ultimately these lead, on the one hand, to optimization of cardiovascular function and, on the other, to changes in type of metabolism and activation of lipid metabolism, while glycolytic activity continues. As a result, a new level of homeostasis is attained, reflected in increased expenditure of energy to perform a given level of exercise with somewhat depressed but stable level of energy efficiency. Cardiovascular changes are retained longer during readaptation, and this increases the efficiency of physical exercise to a level above baseline.

Table 1: Changes in parameters of the human cardiovascular system during adaptation to physical exercise at high altitudes

Table 2: Changes in rate of glycolysis on various substrates and concentrations of hormone during adaptation to physical exercise under hypoxic conditions

Table 3: Oxygen consumption during and after a bicycle ergometer test in subjects at various times during adaptation to high altitudes

Table 2: Efficiency, oxygen pulse, and cardiac cost of work at various times during adaptation to high altitudes

Table 3: Increase in temperature of the femur after a bicycle ergometer test

P1033(22/89)* Aliyev MA, Bekbolotova AK, Lemeshenko VA.
Positive and negative effects of antioxidants on tolerance for hypoxia and thrombocyte aggregation as a function of duration of adaptation to high altitude conditions.
Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.
23(1): 79-81; 1989.
[1 reference; none in English]

Hematology, Thrombocyte Aggregation, Hypoxia, Tolerance
Rats, Male
Adaptation, High Altitude, Pharmacological Countermeasures, Antioxidants

Abstract: This experiment was performed on white male rats. There were 5-6 animals in each condition. Hypoxia tolerance was determined by raising the animals to an altitude equivalent of 12,000 m at the rate of 25 m/sec. Exposure at that level continued until the second gasping breath, after which the animals were lowered. After 5-6 minutes, blood was taken for analysis. Thrombocyte aggregation was determined using an undescribed micromethod. Papaverin (papaverine hydrochloride), novodrin (isoproterenol sulfate), and sodium oxybutyrate were administered 1 hour before the ascent: the first two in a dose of 0.25 mg/100 g, and the last in a dose of 1000 mg/kg. All drugs were administered intraperitoneally.

Standard hypoxic stress is characterized by hyperaggregation and decreased deaggregation. Time to unconsciousness at 12,000 m for control animals was 13.4 min. Papaverin, by inhibiting ADP-aggregation of thrombocytes by more than a factor of 2, increased time to unconsiousness in 3 out of 6 rats. Novodrin significantly increased disaggregation and increased hypoxia tolerance time by more than a factor of 2. Sodium oxybutyrate did not demonstrate any antihypoxic properties. When animals were exposed to an altitude of 1600 m for 10 days, tolerance of hypoxia increased by a factor of 1.5. Both papaverin and novodrin decreased tolerance to hypoxia (by a factor of 2 and 4, respectively) under these conditions. Animals receiving paperin showed greater disaggregation than those receiving novodrin. Under these conditions, sodium oxybutyrate increased hypoxia tolerance by a factor of 1.5. Although animals receiving sodium oxybutyrate lived longer, there were no changes in disaggregation.

In the third condition, animals were exposed to altitudes of 1600 m for 1 year and then tested. With no drugs administered, these animals showed heightened tolerance of hypoxia. Neither novodrin nor oxybutyrate affected hypoxia tolerance under these conditions; however, these drugs did facilitate thrombocyte disaggregation. When animals adapted to 1600 m were moved to 2200 m and adapted to it (not specified for how long), those given no drugs reacted virtually the same way those in the previous condition did. Papaverin had no effect on tolerance time or thrombocyte disaggregation. Novodrin and sodium oxybutyrate decreased tolerance of hypoxia significantly. The authors conclude that the anithypoxic effects of various drugs depend on the degree to which the subject is already adapted to hypoxia.

Table: Changes in the hypoxic tolerance and ADP-aggregation of thrombocytes in rats at sea level given prophylactics of hypoxic stress, papaverin, novodrin, and sodium oxybutyrate at low, moderate, and high altitude equivalents.

BIOLOGICAL RHYTHMS

PAPER:

P1021(22/89)* Dobriyan VV, Shprit MB, Yeroshenko VSh, Abdashimov KA.
Circadian rhythms of blood acetyl cholinesterase in response to hypokinesia and administration of organic phosphates.
Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.
23(1): 31-35; 1989.
[17 references; 7 in English]

Biological Rhythms, Circadian Rhythms; Hematology, Blood Acetyl Cholinesterase
Rats, Male
Hypokinesia, Organic Phosphates

Abstract: Studies have revealed that human and animal tolerance for toxic substances varies with the time of day they are administered. No work has been done to indicate how toxicological sensitivity alters over the course of a day in a subject exposed to hypokinesia, which is considered relevant to space flight. As a model, the present study used organic phosphates administered through cutaneous absorption. Subjects were 240 white male rats studied during various seasons. Dependent variables were activity of acetyl cholinesterases in whole blood (ACE) and rectal temperature. Chronotoxicity was studied in the summer in 48 outbred 3-month-old white male rats divided into 6 groups with 8 subjects in each. The rats were housed in a cage in which microclimate and illumination simulated natural diurnal variations. After 2 days of adaptation, baseline parameters were measured at 10:00, 14:00, 18:00, 22:00, 02:00 and 06:00 in groups 1-6, respectively. After 1 week, the parameters were measured again, but this time in animals undergoing 4 hours of immobilization through restraint. Two weeks later, after 4 hours of immobilization the animals were exposed to 1/25 of LD_{50} of butifos and parameters measured again. Butifos is a pesticide that is rapidly absorbed through intact skin; chemical composition unknown. After 3 weeks 1 LD_{50} was administered. During a recovery period (under which there was no further exposure to immobilization or toxic substances), parameters were again measured after 4 and 5 weeks at the same times of day. After recovery, animals were again immobilized for 4 hours daily 5 days a week for a 4-weeks period and then given 1/5 of LD_{50}. Parameters were measured after 5, 10, and 20 such treatments.

Results on blood acetyl cholinesterases showed a clear desynchronizing effect of immobilization. No 24-, 12-hour or shorter cycles could be identified. Administration of 1/25 LD_{50} to immobilized rats introduced a synchronizing effect, with ultradian components predominating. Increasing dose to 1 LD_{50} did not alter the 24-hour component, but disrupted ultradian components. Repeated administration of the toxic substance in immobilized rats decreased and eventually eliminated the 24-hour rhythm, with the 12-hour rhythm being retained. Immobilization appeared to trigger a rhythmic process in rectal temperature, while the first toxic dose disrupted it. Increasing the toxic dose appeared to again trigger a rhythm with diurnal components predominating. Ultradian components characterized the recovery process. Correlation analysis of effects on blood ACE and rectal temperature rhythms revealed a range of +0.8 (at a dose of 1 LD_{50} and immobilization) to -0.8 (at an accumulated dose of $2LD_{50}$).

Table 1: Chronotoxicity of butifos administered through skin in immobilized rats(blood ACE)

Table 2: Chronotoxicity of butifos administered through the skin in immobilized animals (rectal temperature)

MONOGRAPH:

M144(22/89) Zidermane AA (editor) [Зидермане]
Nekotoryye voprosy khronobiologii i khronomeditsiny: Obzor literatury
Некоторые вопросы хронобиологии и хрономедицины: Обзор литературы
Some issues in chronobiology and chronomedicine: A review of the literature.
Riga: Zinatne; 1988.
[214 pages; 997 references; 5 tables; 5 figures]

KEY WORDS: Biological Rhythms, Chronopathology, Chronopharmacology, Drugs,Endocrinology, Biochemistry, Cardiovascular and Respiratory Systems, Neurophysiology

Annotation: This book is the first Soviet review of modern data in chronopathology and chronopharmacology. It discusses the chronopathology of biochemical reactions, chronotoxicology, chronotherapy of inflammatory and cardiovascular disease, and also the chronopharmacology of the central nervous system.

The mechanism underlying "biological hours" is considered, starting at the level of the cell and organ up to the level of chronobiological rhythms in hormonal regulation and the activity of the central nervous system.

The author demonstrates the need to correctly evaluate functional status of humans under normal and extreme conditions and pathology, and also to consider biological rhythms in developing schedules for chemotherapy.

CONTENTS

BIOSPHERICS

PAPERS:

P1024(22/89)* Levina RV, Smirnov RV, Olimpiyenko TS.
The effects of a hypogeomagnetic field on warm-blooded animals.
Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.
23(1):145-47:1989.
[10 references; 3 in English]

Biological Effects, Radiobiology, Cardiovascular and Respiratory Systems, Physical Work Capacity, Psychology, Behavioral Measures, Learning
Rats, Males
Biospherics, Geomagnetic Field, Hypoexposure

Abstract: In this study, a total of 90 mature male Wistar rats were housed in one of three chambers. The first provided normal exposure to the Earth's magnetic field. The other two were constructed of permalloy and attenuated the Earth's magnetic field by factors of 2.5 (20 μT) and 172.5 (0.29 μT) for groups 2 and 3, respectively. Throughout the experiment temperature, humidity and illumination conditions in all three chambers were identical. The animals were given ordinary laboratory feed on a typical schedule. Animals were confined in the chambers for 3 months (November, December, and January). Dependent variables were EKG, physical work capacity, endurance, behavioral activity, and ability to learn. Endurance and work capacity were measured by recording the amount of time an animal could swim while carrying a weight 10% of body weight. A coefficient of fatigue was computed for work capacity. This coefficient was the ratio of time taken to swim out of the water on the last 10 of 30 trials to the time required during the first 10 trials. Endurance was identified with the amount of time the animal could keep afloat. Activity was measured using the "open field test." Learning ability was measured through teaching an instrumental pedal-pushing response to obtain food.

Group 2 showed no cardiovascular differences from the control. Group 3, with the lowest exposure to the Earth's magnetic field, displayed increased heart rate, which, while significantly different from the control, was within normal limits. Coefficient of fatigue for group 2 did not differ from control level. It was not possible to compute a coefficient for group 3 because only one animal of the group completed 30 swimming trials, while the others started to drown completing fewer than 20 trials. Animals in group 3 were able to remain above water for less than one quarter the time of control animals. Activity level of group 2 animals was slightly below that of control; activity level of group 3 animals was less than one quarter that of controls. Time to learn a conditioned food response was slightly below that of control animals in group 2 and very significantly below control in group 3. Animals in group 3 were found on dissection to display pathological changes in the lungs .

Table 1: Changes in some physiological parameters in experimental rats after 3 months of exposure to low magnetic environments

Table 2: Distribution of animals with respect to activity levels and time to develop a conditioned reflex

BODY FLUIDS

PAPER:

P994(22/89) Bukayev YuN.
Physical exercise and renal function.
Teoriya i praktika fizicheskoy kul'tury.
1988(12): 36-37.
[8 references; 5 in English]

Body Fluids, Renal Function, Cardiovascular and Respiratory Systems, Renal Hemodynamics
Humans, Athletes
Physical Exercise, Long-Term Effects

Abstract: This study investigated the effects of intense and sometimes extreme physical exertion lasting a number of years on the status of the urinary system. Renal function was studied in 44 highly qualified athletes after they had ceased training for from 5 days to a year and longer. Functional changes were investigated using radioisotope renography, as well as excretory urography, and ultrasound and biochemical studies to exclude organic and innate kidney abnormalities. Abnormality of one or more isotope renographic parameters was noted in a large majority (70.4%) of those studied. Time to excrete a labelled substance, which reflects the passage of urine through the upper urinary tract, was increased in 22 (of 44) patients. Clearance fluctuated from 17 to 82% of normal. Decreased purifying capacity was observed in 63.6%, while decrease in effective renal plasma flow was noted in 69.9% of the cases. The author argues that the major reason for functional changes in the kidney in response to prolonged intense exercise is the adaptive hemodynamic response to exercise -- redistribution of circulation and subsequent decrease in renal blood flow and ischemization of the organ. The data obtained here refute the idea that the functional and structural changes that occur in the kidney in response to exercise disappear completely. The changes persist in a high percentage of athletes, even after long periods without intense exercise.

Table: The effect of multiyear intense exercise on the functional state of the kidneys

CARDIOVASCULAR AND RESPIRATORY SYSTEMS

PAPERS:

P982(22/89)* Yegorov AD. Bayvskiy RM, Itesekhovskiy OG, Fedorov BM, Turchaninova VF, Alferova IV, Lyamin VR, Turbasov VD, Polyakova AP, Domracheva MV, Golubchikova ZA, Funtova II, Tazetdinov IG, Savelyeva VG.
Preliminary results of investigation of the cardiovascular system in members of the second prime crew on space station Mir.
Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.
22(6): 51-58; 1988.
(14 references; none in English)

Cardiovascular and Respiratory Systems
Humans, Cosmonauts, Prime Crew
Space Flight, Mir, Long-Term, Provocative Tests, Exercise, LBNP

Abstract: This paper presents the results of cardiovascular studies performed on three members of the second Mir prime crew. The Mir crew consisted of commander, Yu.V Romanenko (age 43, two previous flights of 96 and 8 days, Mir flight duration 326 days); the first flight engineer, A.I. Laveykin (age 36, replaced after 175 days); and second flight engineer, A.P. Aleksandrov (age 44, one previous flight of 150 days, Mir flight duration 160 days). The goal of the study was to investigate the functional status of the circulatory system during long-term exposure to weightlessness, while cosmonauts were at rest or performing provocative tests involving graded physical exercise on a bicycle ergometer or lower body negative pressure. Onboard apparatus were used to obtain electro-, seismo-, ballisto-, and kinetocardiograms to provide information about mechanical cardiac functioning In addition, impedance plethysmograms were recorded for the trunk, head, forearm, and calf; sphygmograms were made of the temporal, femoral, radial, and anterior femoral arteries; phlebograms were taken in the area of the right jugular vein; and tachyoscillograms wree made of the brachial artery. Blood pressure was measured as well. Data were transmitted to Earth for analysis. The following parameters were measured:

EKG: temporal and amplitudinal parameters, frequency and pattern of cardiac rhythm;
Phlebogram of the jugular veins and kinetocardiogram: phases in activity of the right and left hearts (auricular systole, isometric contraction phase, ejection period of the ventricle, protodiastolic interval, isometric relaxation phase; rapid and slow filling of the ventricle);
Seismocardiogram: amplitude of the first fluctuation cycle and its ratio to the second cycle, indicative of cardiac work;
Ballistocardiogram: amplitude of systolic segments and their ratios;
Impedance plethysmogram of the trunk: cardiac stroke and minute volumes;
Impedance plethysmogram of the head and limbs: pulsed filling of the vessels; duration of anacrotic pulse and of the whole cycle, reflecting tonus of large arteries, dicrotic index (ratio of amplitude at the level of the incisura to the maximum amplitude of the curve), characterizing tonus of pre- and postcapillary vessels;
Temporal pulsogram and peripheral sphygmograms: tonus of major vessels; tonus of peripheral arteries and veins;
Tachyoscillogram of the brachial artery (while blood pressure was measured): minimal, mean, true systolic, end systolic, and true pulse pressure of a hemodynamic stroke;

Plebogram of the jugular veins: phase structures, degree of filling of the jugular veins.

Derived parameters included an index of activity of regulatory systems and a composite reflecting activity of adrenergic and cholinergic mechanisms. Graded physical exercise on a bicycle ergometer pre- and inflight followed a schedule of 125 W for 5 minutes, rest for 1 minute, 175 W for 3 minutes, rest for 5 minutes. LBNP was created using a suit with a decompression schedule of -25, -35, and -45 mm Hg for 1, 3 and 3 minutes, respectively.

Bioelectric activity of the myocardium. All crewmembers displayed a sinusoidal rhythm. Heart rate corresponded to the mean preflight values for two crewmembers, while one displayed increased heartrate starting from month 1. Episodes of extrasystole occurred in two cosmonauts at rest. Mathematical analysis revealed that before days 97-100 of flight, the regulatory index indicated relative regulatory stability with a slight predominance of the sympathetic nervous system in one cosmonaut The second showed clear dominance of the parasympathetic system, while the third displayed marked sympathetic dominance. All crewmembers showed a diffuse decrease in the amplitude of the T wave, particularly in left leads. In one crewmember, the T wave had decreased by 13-60% at the end of month 2 and subsequently spread to the majority of leads. This was combined with deformations of the T wave. Results with provocative tests suggested that these disturbances were functional. After physical exercise therapy and administration of riboxin (chemical composition unknown), panangin (potassium and magnesium asparaginate), and potassium orotate, these changes tended to normalize. One subject (Laveykin) showed serious EKG disruption. Extrasystoles began to occur at rest during week 2. During subsequent EVA activity frequent extrasystoles and episodes of trigeminy were noted. Extrasystolic arrythmia also occurred during provocative exercise tests on the treadmill. To forestall increases in the severity of cardiac problems, this crewmember was replaced before the scheduled end of his flight.

Mechanical cardiac function. During the flight, patterns of change in ballisto- and seismocardiograms differed from individual to individual. Analysis of the data concerning the parameters of external and overall cardiac work suggests that as the cardiovascular system adapts to space flight, energy characteristics alter, while hemodynamic balance is maintained.

Hemodynamics. During flight, all crewmembers showed a tendency for diastolic pressure to decrease, and for pressure in the pulmonary artery to increase; instability of blood filling parameters in the jugular veins was also observed. Cardiac minute volume decreased in two subjects and increased in one. Phase structure analysis indicated a lengthening of the isometric relaxation phase in the right ventricle in all crewmembers, which in two out of three cases was accompanied by shortening of the duration of the analogous phase in the left ventricle. Impedance plethysmography revealed the following general tendencies: decrease (especially on the right) in tonus of cerebral vessels and development of asymmetry with signs of impeded venous outflow, as indicated by appearance of marked venous waves; decreased tonus of vessels in the arms; decreased pulsed blood filling of the vessels of the calf, accompanied by increase in their tonus. There were a number of additional individual effects. One cosmonaut showed decreased mean, true, and pulsed systolic blood pressure and hemodynamic stroke volume, as well as decreased cardiac minute volume. At some points during the flight, he showed signs of increased volume pressure on the left heart. At most points during flight there were signs that blood filling had increased in his jugular veins. There was a clear tendency for the tonus of small peripheral vessels to decrease and the tonus of large arteries, especially in the legs, to increase. This subject also showed increased pulsed filling of vessels of the brain and basin of the internal carotid arteries, and more pronounced decrease in pulsed filling of the vessels of the calves than did the others. Another crewmember showed signs of vagotony at rest pre- and inflight, as manifested in decreases in heart rate and all blood pressure parameters (except end systolic), appearance of the phase syndrome of myocardial hypodynamia, and increased stroke and cardiac minute volume. This cosmonaut showed more pronounced increases in blood filling of the jugular veins and pressure in the pulmonary artery. He also displayed the most pronounced asymmetry in pulsed blood filling of cerebral vessels (decrease in the right hemisphere and increase in the left) and a relatively insignificant decrease in pulsed filling of the vessels in the calf. The third crewmember showed a tendency for heart rate to increase at rest and a decrease in diastolic pressure; this was accompanied by a tendency for true systolic pressure and hemodynamic stroke to increase. He also displayed marked fluctuations in parameters related to blood filling of the jugular veins.

Graded physical exercise test. For the first crewmember, tolerance of the exercise tests was good throughout. Although tests did induce greater increase in systolic blood pressure than occurred on the ground, diastolic blood pressure remained relatively low. Increase in end systolic pressure was due more to decreased elasticity of the walls of major vessels than increased myocardial contraction strength. By day 280 physical work capacity had increased. In the second crewmember, exercise tolerance decreased during the course of the flight. This was manifest in a pronounced increase in heart rate and decrease in physical work capacity. During an exercise test on day 13, this cosmonaut developed a hypertensive reaction to exercise.. In a number of instances, hemodynamic recovery after exercise was slowed. Systolic hypertension and increased cardiac minute volume were more severe in response to exercise than preflight. The third cremember also displayed heightened tachycardia and diminished physical work capacity during the majority of inflight exercise tests.

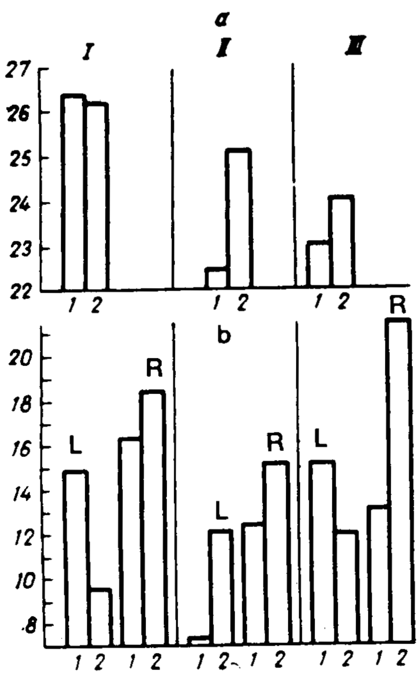
Lower body negative pressure (LBNP) tests. The first crewmember tolerated all tests well, displaying no substantial changes compared to preflight responses. The second crewmember also displayed an appropriate hemodynamic response, although low pulsed blood filling and cerebral vascular tonus parameters indicated that LBNP did not exert a normalizing influence on vascular tonus, as in the majority of cosmonauts. The third crewmember showed greater increase in heart rate in response to LBNP than preflight. Hemodynamic parameters did not differ significantly from preflight parameters.

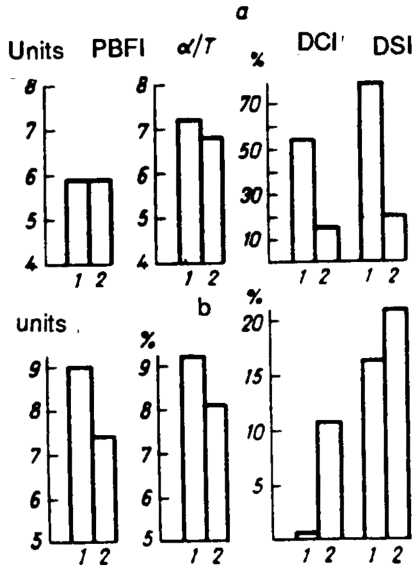
The authors conclude that their results show that it is possible to spend 11 months in space and still maintain high levels of functional stability in the circulatory system. One crewmember did experience an intensification of the vagotony noted preflight, while another displayed changes in hemodynamics typical of response to weightlessness, although changes in regional hemodynamics were more variable than usual. Thus during long-term space flight changes in parameters of the cardiovascular system are, to a great extent, determined by individual differences in how the body reacts to weightlessness and other flight factors. All these changes do not exceed normal variations. However, support of normal levels of cardiovascular functioning in space requires expenditure of functional reserves and stresses the regulatory systems. Preliminary analysis of the data obtained shows that the "energy cost" of maintaining hemodynamic balance appropriate to space flight may be maintained with minimal stress on the autonomic regulation system, as occurred in one crewmember (Romanenko). In the second crewmember, due to individual characteristics of response to flight there was a significant increase in parasympathetic effects on the ino- and chronotropic function of the heart. In the third crewmember, due to a pronounced shift of autonomic homeostasis in the direction of sympathetic dominance, the energy cost of hemodynamic balance was higher than for the other two.

Table: Changes in major hemodynamic parameters at rest in members of the second prime crew pre- and in-flight

Cosm- naut	Para- meter	Preflight mini-	maxi-	mean	Month inflight 1	2	3	4	5	6	7	8	9	10	11
I	HR	59	69	65	61	63	64	63	64	63	62	65	61	63	66
	BP_{dias}	64	88	72	60	—	50	50	55	62	62	56	66	63	62
	BP_{endsys}	126	145	130	139	—	139	130	135	144	137	132	137	141	147
	SV	91	115	104	120	79	101	79	98	97	100	89	84	104	103
	CMV	6.2	7.6	6.8	7.0	4.8	6.6	4.9	6.0	5.7	6.0	6.0	5.2	6.5	6.9
	BFJV	83	135	106	106	109	95	100	104	115	112	117	100	111	88
II	HR	44	52	48	45	49	49	48	53	50	—	—	—	—	—
	BP_{dias}	45	62	56	50	—	43	49	45	53	—	—	—	—	—
	BP_{endsys}	107	124	118	116	—	114	116	118	111	—	—	—	—	—
	SV	96	138	118	132	—	143	122	132	129	—	—	—	—	—
	CMV	4.3	6.5	5.6	6.1	—	6.6	5.4	7.2	5.8	—	—	—	—	—
	BFJV	76	136	117	145	121	119	154	105	—	—	—	—	—	—
III	HR	52	65	58	61	67	72	66	78	—	—	—	—	—	—
	BP_{dias}	62	74	67	56	62	—	62	61	—	—	-	—	—	—
	BP_{endsys}	118	136	125	113	123	—	134	129	—	—	—	—	—	—
	SV	67	129	99	80	87	—	—	85	—	—	—	—	—	—
	CMV	4.3	7.2	5.6	5.1	5.6	—	—	6.9	—	—	—	—	—	—
	BFJV	29	107	96	115	95	—	107	91	—	—	—	—	—	—

Key: HR - heart rate; BP_{dias} - diastolic blood pressure, mm Hg; BP_{endsys} - end systolic blood pressure, SV - stroke volume, ml; CMV - cardiac minute volume - l/min; BFJV - index reflecting blood filling of jugular veins, %





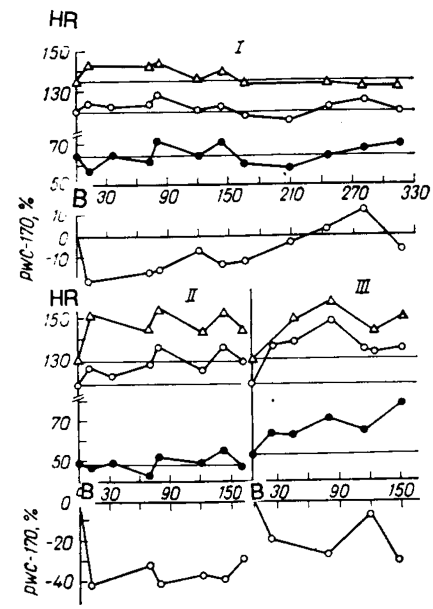


Figure 1: Changes in stress index for the left ventricle (a) and relaxation of the left and right ventricles (b) of the myocardium in members of the second prime crew at rest pre- (1) and in-flight (2) (mean values)

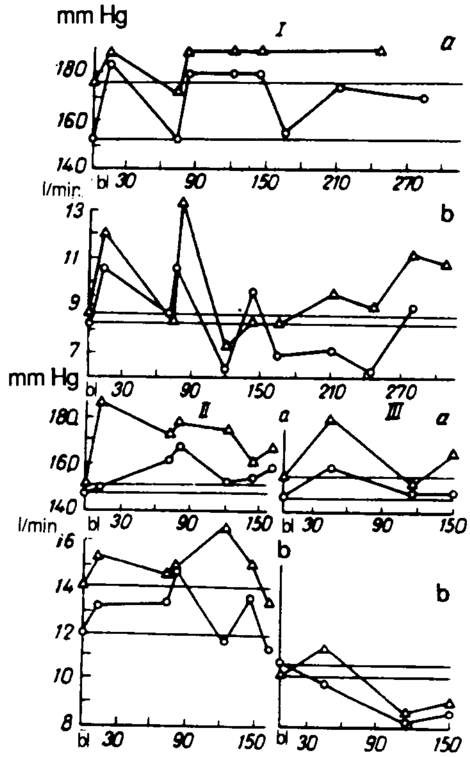
L - left ventricle; R - right ventricle; Here and in Figure 3 -5, I, II, and III refer to subjects.

Figure 2: Changes in impedance plethysmography parameters of the forearm (a) and calf (b) in members of the second prime crew at rest pre- (1) and in-flight (2) (mean values)

PBFI - pulsed blood filling index of vessels; α/T - ratio of duration anacrotic pulse to duration of entire cardiac cycle; DCI - dicrotic index; DSI - diastolic index.

Figure 3: Changes in heart rate and parameters of physical work capacity (PWC-170) during graded physical activity on a bicycle ergometer in members of the second prime crew pre- and inflight

Filled and empty circles and triangles - heart rate before and during first and second levels of exercise, respectively; circles with dots [sic., not indicated in figure]- PWC-170; horizontal line - averaged preflight levels of parameters; BL - mean baseline parameter value; abscissa - time, days.



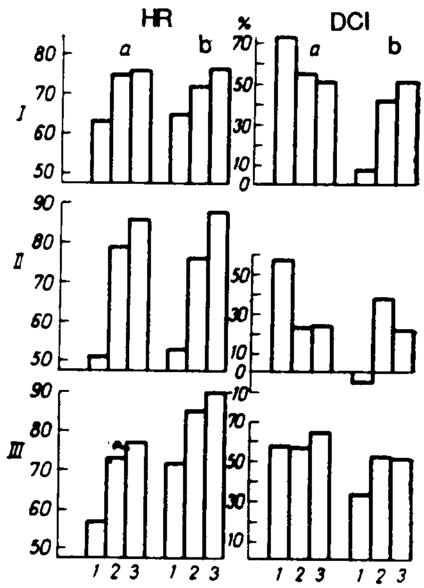


Figure 4: Changes in end systolic blood pressure (a) and cardiac minute volume (b) immediately after exercise on bicycle ergometer in members of the second prime crew pre- and inflight

Key: as in Figure 3

Figure 5: Changes in heart rate and dicrotic index on impedance plethysmogram of the head in response to LBNP in members of the second prime crew pre- (a) and inflight (b)

1 2, 3 - respectively, pre-LBNP, during LBNP of 35 mm Hg, during LBNP of 45 mm Hg

DEVELOPMENTAL BIOLOGY

PAPERS:

P1004(22/89) Serova LV, Chel'naya, Bryantseva LA.
Structure and metabolism of the organs of animals at various stages of postnatal ontogeny: General state of the animals. Body and organ weight. Blood profile.
In: Gazenko OG (editor). Ontogenez mlekopitayushchikh v nevesomosti ***[Ontogeny of mammals in weightlessness.]***
Moscow: Nauka: 1988. Pages 112-114.

Developmental Biology, Postnatal Ontogeny, Growth, Body Weight, Liver, Kidney, Endocrinology, Thymus, Adrenal Gland; Hematology, Blood Profile
Rats, Neonates
Space Flight, COSMOS-1514

Abstract: Observations of rats exposed to space during days 13-18 of prenatal ontogeny on COSMOS-1514, with synchronous and vivarium controls, showed that, in general, the rats were active and ate well. Only two rats (one from the flight group and one from the vivarium control group) showed signs of listlessness, loss of appetite, and delay in weight gain; after dissection on day 30 these animals were both found to have had pneumonia. Some animals in all three groups were dissected on days 15, 30, and 100 of their lives for study of the structure and metabolism of their visceral organs and musculoskeletal system. On day 15, only female rats were dissected, and on days 30 and 100 only males. Aside from the two cases noted above, no pathological changes were observed in the visceral organs No differences were found between the experimental and control groups in the absolute or relative (in proportion to body weight) weight of visceral organs at any point. he relative and absolute weights of the thymus, adrenal gland, liver, and kidneys were virtually identical in all three groups.

Hematological studies of animals developing under conditions of weightlessness are of particular interest at various stages of the postnatal period. Particularly important are studies of the erythrocyte system, which is highly sensitive to the effects of weightlessness, especially since postflight examinations of female rats exposed to microgravity during pregnancy revealed signs of anemia and decreased concentration of colony forming units (CFUs) in bone marrow. In neonate rats developing under conditions of weightlessness, concentrations of hemoglobin and reticulocytes in blood also showed a tendency to decrease; differences from the control group were reliable However, when the rats were examined on day 15 of life, no differences were found from the control groups in hemoglobin concentration of hemoglobin. Examinations on days 30 and 100 revealed that concentration of hemoglobin in the blood of the experimental animals was even higher than in the control group. The difference between the groups was slight, but statistically reliable (Table 35). At no observation point were there significant differences between the experimental and control groups in concentration of reticulocytes or leukocytes or the percentage composition of lymphocytes and neutrophils with segmented nuclei in peripheral blood.

Table 35: Postnatal ontogeny. Peripheral blood profile.

Age, days	Grp	Hemoglobin, g %	Lymphocytes 1000/mm3	Neutrophils, 1000/mm3 segmented	bacillar-nuclei	young nuclei	Reticulocytes. %
15	F	8.2±0.49	2.6±0.22	0.7±0.22	0.2±0.009	0.1±0.01	
	SC	7.8±2.8	1.9±0.3	1.5±0.6	0.2±0.07	0.1±0.07	
	VC	8.4±0.19	2.8±0.5	1.4±0.8	0.2±0.08	0.2±0.8	
30	F	12.2±0.27*	6.8±1.46	1.5±0.30	0	0	293±7.7
	SC	11.3±0.3	5.4±0.73	1.4±0.19	0.1	0	326±8.1
	VC	10.9±0.09	5.6±0.73	1.2±0.45	0	0	305±7.5
100	F	12.8±0.31*	8.8±0.23	2.5±0.8	0	0	56±1.7
	SC	10.9±0.27	9.9±1.3	3.7±0.6	0	0	55±2.3
	VC	11.0±0.36	10.1±1.9	3.14±0.8	0	0	56±2.3

* difference between experimental and both control groups significant, $p < 0.01$

P1005(22/89) Yurchovichova Ya., Yezhova D, Bigash M (Czechoslovakia), Serova LV (USSR).
Structure and metabolism of the organs of animals at various stages of postnatal ontogeny: Concentration of hormones in blood plasma.
In: Gazenko OG (editor). Ontogenez mlekopitayushchikh v nevesomosti ***[Ontogeny of mammals in weightlessness.]***
Moscow: Nauka: 1988. Pages 114-115.

Developmental Biology, Postnatal Ontogeny; Endocrinology, Prolactin, Somatropin, Insulin, Corticosterone
Rats, Neonates
Space Flight, COSMOS-1514

Abstract: On days 15, 30,and 100 of the lives of rats developing under conditions of weightlessness, concentrations of hormones were measured in their blood plasma. Prolactin and somatropin were measured through radioimmunoassay using a specific antibody or activated charcoal to separate the free from the bound hormone. Corticosterone was measured through protein binding and insulin through radioimmunoassay. The results obtained are presented in Figure 40.

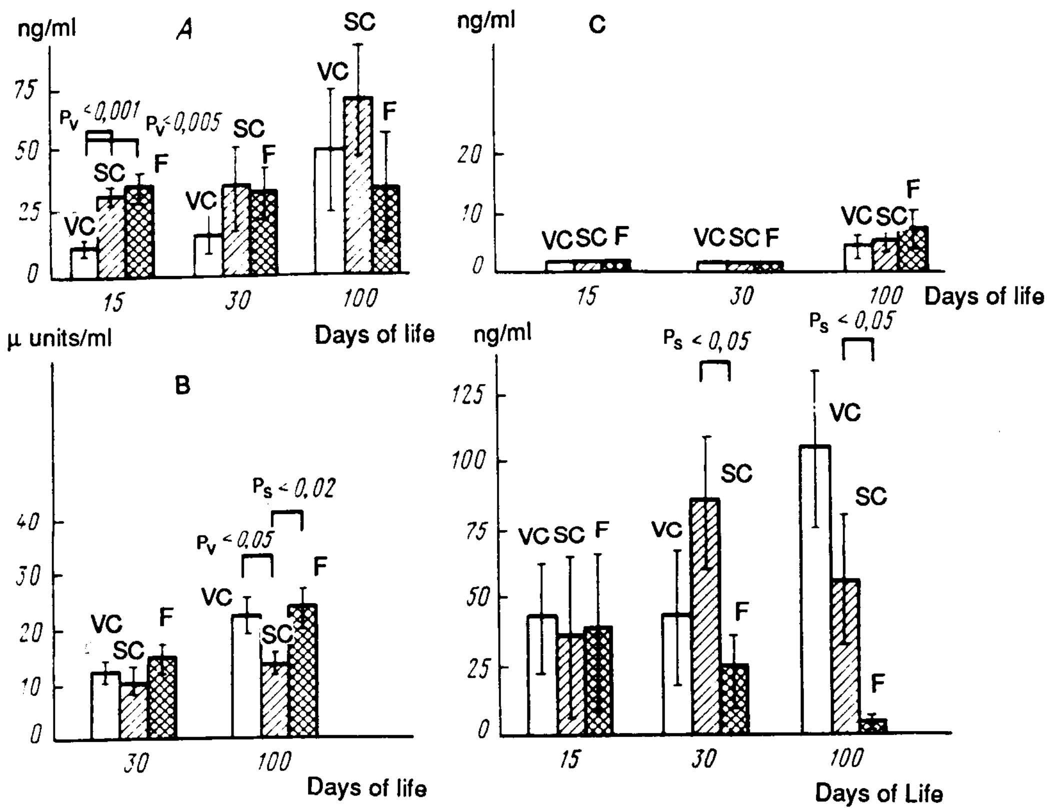


Figure 40 Postnatal ontogeny. Concentrations of corticosterone (A), insulin (B), prolactin (C) and STH (D) in blood plasma

P1006(22/89) Kvetnyanski R, Bazhichek P, Makho A. (Czechoslovakia). Serova, LV (USSR). ***Structure and metabolism of the organs of animals at various stages of postnatal ontogeny: The sympathetic adrenal system.***
In: Gazenko OG (editor). Ontogenez mlekopitayushchikh v nevesomosti ***[Ontogeny of mammals in weightlessness.]***
Moscow: Nauka: 1988. Pages 115-117.

Developmental Biology, Postnatal Ontogeny; Endocrinology, Sympathetic Adrenal System
Rats, Neonates
Space Flight, COSMOS-1514

Abstract: Information was obtained on the state of the sympathetic adrenal system of experimental (prenatally exposed to space) and control rats at various stages of postnatal development by studying metabolism of catecholamines in the adrenal glands and catecholamine concentrations in blood plasma. Adrenaline and noradrenaline were measured using method cited in Peuler and Johnson (1977, not described), and activity of phenylethanol amine-N-methyltransferases using Axelrod's method (1962, not described).

When rats are born, sympathetic innervation of the peripheral organs is absent or nonfunctional, and the secretion of catecholamines by the cortical layer of the adrenal glands is mainly an adrenergic effect. Since the splanchic nucleus, which to a significant extent regulates the activity of the cortical layer of the adrenal gland, does not start to function before the end of the first week of postnatal development, secretion of noradrenaline is not triggered neurogenically, but through some other mechanism. Data in the literature testify to the significant role of catecholamines in the capacity of neonates to endure stress.

In the present experiment, animals spending a portion of their prenatal period under conditions of weightlessness were studied on days 15, 30, and 100 of their lives and compared to the appropriate controls.

Results of this study for adrenaline, noradrenaline and dopamine in the adrenal glands are presented in Figure 41. The level of noradrenaline in the flight group at 100 days was significantly greater than in either control ($p<0.05$). The concentration of dopamine in the adrenal glands at all points of observation was virtually identical in the flight and vivarium control groups, while in the synchronous control it was significantly depressed on days 30 and 100.

The activity of tyrosine hydroxylase — the key enzyme in the synthesis of catecholamines i— and of Phenylethanolamine N-Methyltransferase remained identical in all three groups at all observation points).

It should be noted that the age-related changes found in the concentration of catecholamines in the adrenal glands and the activity of its synthesis enzymes in the animals of the vivarium control group correspond to previous results The totality of data obtained suggest that 5 days of prenatal exposure to weightlessness during the last third of pregnancy, which induced pronounced changes in the mothers did not affect the adrenal glands in their progeny at various stages of postnatal ontogeny.

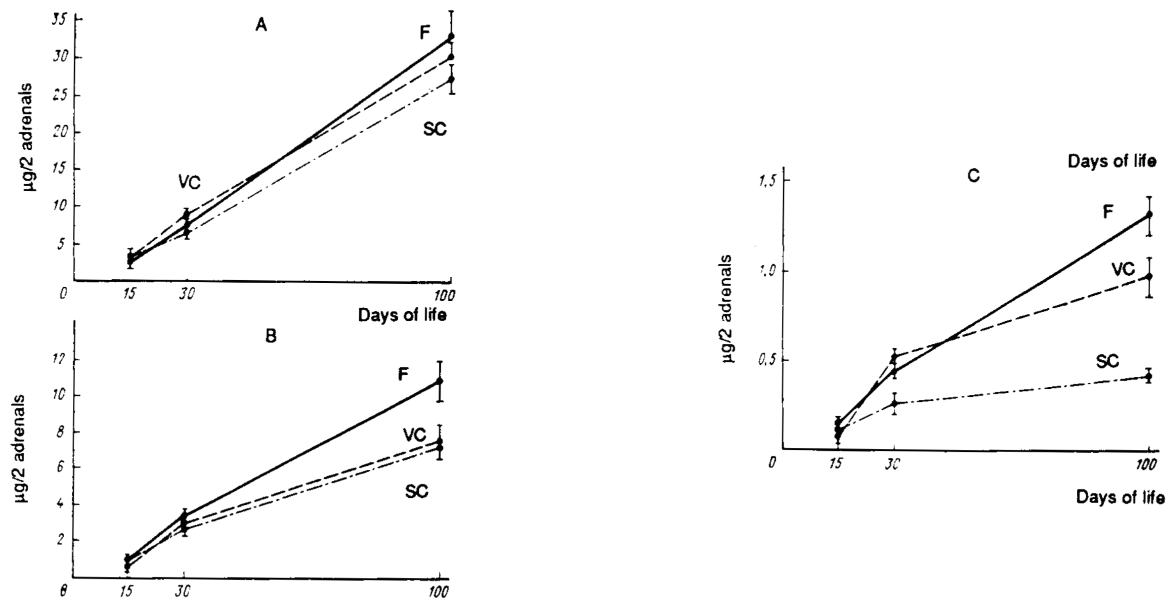


Figure 41: Postnatal ontogeny. Concentration of adrenaline (A), noradrenaline (B), and dopamine (C) in the adrenal glands.

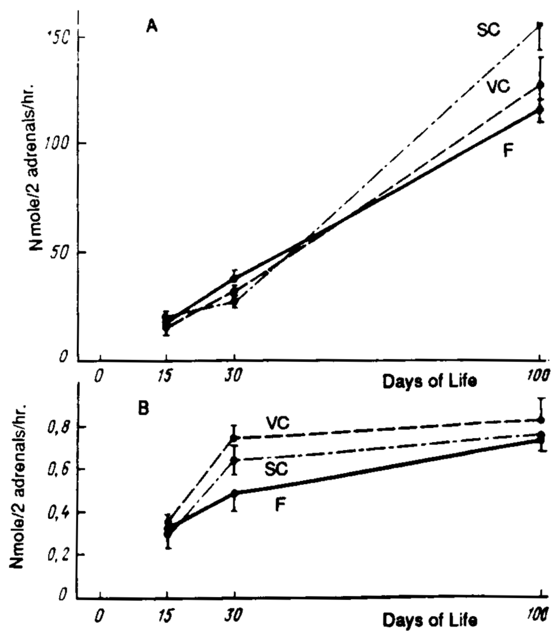


Figure 42: Postnatal ontogeny. Activity of tyrosine-hydroxylase (A) and phenylethanolamine N-methyltransferase (B) in the adrenal gland

P1007(22/89) Knopp Ya, Brtko Ya (Czechoslovakia), Serova LV (USSR).
Structure and metabolism of the organs of animals at various stages of postnatal ontogeny: Thyroid gland.
In: Gazenko OG (editor). Ontogenez mlekopitayushchikh v nevesomosti ***[Ontogeny of mammals in weightlessness.]***
Moscow: Nauka: 1988. Pages 117-118

Developmental Biology, Postnatal Ontogeny; Endocrinology, Thyroid
Rats, Neonates
Space Flight, COSMOS-1514

Abstract: The state of the thyroid gland in animals exposed to space during days 13-18 of prenatal development and in appropriate control groups was determined at various stages of postnatal ontogeny on the basis of the concentration of thyroxin and triiodothyronine in thyroid tissues. Thyroid tissue was homogenized in a buffer solution. Complete hydrolysis was achieved using the enzyme pronase. One drop of toluene was added and the substance was incubated while being stirred for 16 hours at 37°. After hydrolysis samples were diluted with a buffer solution and radioimmunoassay was used to measure concentrations of triiodothyronine and thyroxin. Lowry's method was used to measure hormone concentrations per 1 mg protein. Results are presented in Table 36.

Table 36: Postnatal ontogeny. Concentration of triiodothyronine and thyroxin in the thyroid gland

Age	Group	Triiodothyronine, µg/mg protein		Thyroxin, µg/mg protein
15	F	0.02±0.005	$p_{V,S} < 0.025$	0.25±0.05
	SC	0.04±0.004		0.14±0.04
	VC	0.04±0.004		0.20±0.02
30	F	0.02±0.006	$p_S < 0.05$	0.08±0.02
	SC	0.06±0.013	$p_V = 0.05$	0.26±0.11
	VC	0.03±0.04		0.12±0.04
110	F	0.18±0.04		0.27±0.12
	SC	0.20±0.004		0.23±0.08
	VC	0.08±0.04		0.15±0.08

P1008(22/89) Batsek A, Bartonichkova A, Rotovska D. (Czechoslovakia); Michurina TV, Domaratskaya YeS, Serova LV (USSR)

Structure and metabolism of the organs of animals at various stages of postnatal ontogeny: Hemopoietic stem cells.

In: Gazenko OG (editor).Ontogenez mlekopitayushchikh v nevesomosti ***[Ontogeny of mammals in weightlessness.]***
Moscow: Nauka: 1988. Pages 118-120

Developmental Biology, Postnatal Ontogeny; Hematology, Stem Cells, Hemopoiesis
Rats, Neonates
Space Flight, COSMOS-1514

Abstract: Concentration of hemopoietic stem cells was measured in the spleens and bone marrow of animals exposed to weightlessness *in utero* Bone marrow from the femurs and spleens of the animals were homogenized and injected intravenously in rat recipients, irradiated at a dose of 9.0 Gy 2 hours before the transplant. The number of stem cells in the suspension were computed in relation to the total number of tissue cells. On day 111 after the transplants, the spleens of the recipients were isolated, fixed in a Carnow solution, and the number of macroscopically visible cell colonies counted on its parietal surface.

In 18-day-old fetuses, the quantity of stem cells in the liver, which is the major hemopoietic organ at this age, averaged 8.2 per 10^6 cells in the flight group, 10.5 in the vivarium and 13.4 in the synchronous control group ($p < 0.05$); at the moment of birth there was no longer any difference between the flight and vivarium control group. Concentration of CFUs in liver tissue was 9.5 per 10^6 in the experimental group and 10.3 in the vivarium control.

In the spleens of neonates of the flight group, the concentration of CFUs was elevated and averaged 19.2 per 10^6, while the corresponding value was 10 in the vivarium and 8.5 in the synchronous control ($p<0.001$). During their first 15 days of life, the number of splenocytes in control animals increased sharply (Figure 43), while in the experimental animals this parameter remained virtually unchanged, so that at 15 days the total number of CFUs in the spleens of experimental rats was significantly lower than in both control groups ($p < 0.02$). However, the relative concentration of CFUs was equal in the experimental and synchronous control groups (Figure 37). At subsequent measurement times, differences in number of splenocytes and absolute and relative number of CFUs were no longer significant.

Study of the bone marrow of the juvenile rats was begun when they were 15 days old. At this time the quantity of CFUs in 10^6 karyocytes in the experimental group was significantly lower than in both control groups (Table 37), but due to the greater quantity of karyocytes, the total number of CFUs in bone marrow of the femur was virtually the same in all three groups (Figure 44). Between days 15 and 100 of their lives, the number of karyocytes steadily increased, remaining virtually the same in the experimental and control groups. At days 30 and 100, no reliable intergroup differences were found in concentration and total number of CFUs in bone marrow (Table 37, Figure 44).

Thus exposure to weightlessness during pregnancy was accompanied not only by changes in the number of hemopoietic stem cells in female rats of the flight group, but also by some degree of instability in this system in their progeny during the prenatal and early postnatal periods. The differences between groups were maintained until the rats were 15 days old and were completely compensated for by the end of their first month of life. At this time and later — at the end of their third month of life — no reliable differences were found in any of the parameters studied.

Table 37: Postnatal ontogeny. Concentration of CFUs in bone marrow and spleen (in 10^6 karyocytes)

Age	Group	Concentration of CFUs: Bone marrow	Spleen
15	F	4.6±0.6 (pv<0.05; ps=0.002)	5.4±0.9 (pv<0.01)
	SC	9.1±0.8	6.0±0.4 (pv<0.001)
	VC	8.9±1.4	10.0±0.6
30	F	14.9±0.8	9.6±0.7
	SC	13.1±1.2	7.8±0.4
	VC	16.3±1.04	8.0±0.6
100	F	15.5±1.2	3.6±1.1
	SC	13.5±1.8	1.2±0.3
	VC	12.4±0.9	2.1±0.8

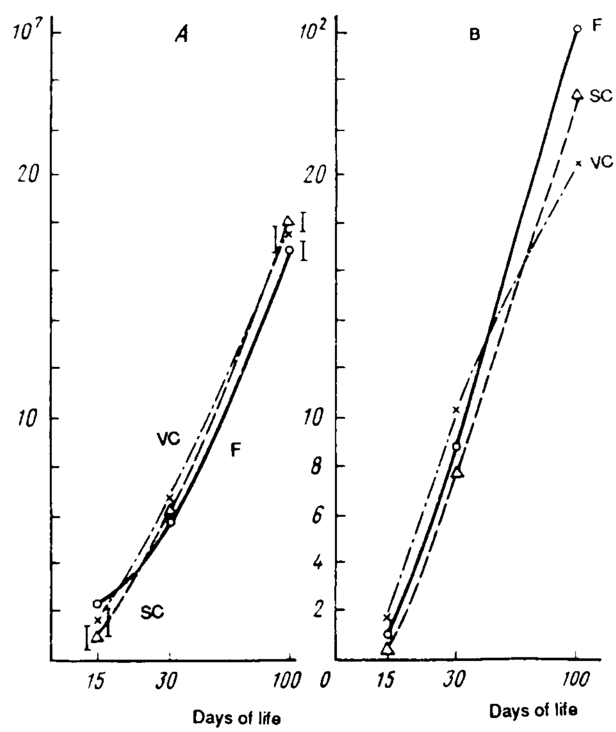


Figure 43: Postnatal ontogeny. Number of splenocytes (A) and CFUs (B) in the spleen

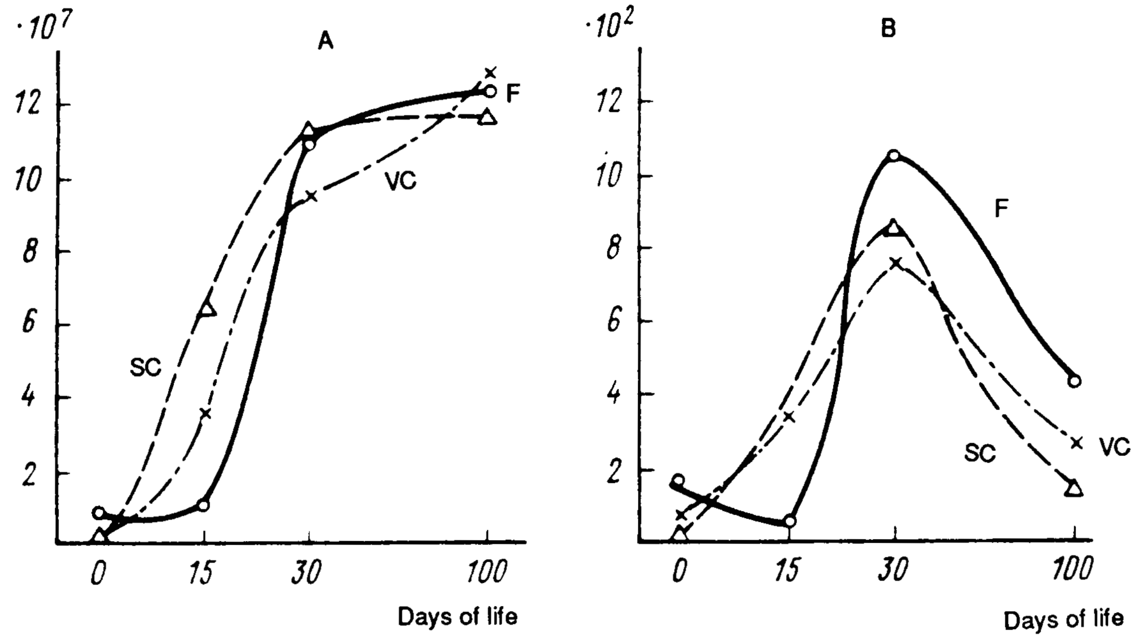


Figure 44: Postnatal ontogeny. Number of karyocytes (A) and CFUs (B) in bone marrow

P1009(22/89) Denisova YeA, Lavrova YuV, Natochin LV, Serova LV, Shakhmatova YeI (USSR)
Structure and metabolism of the organs of animals at various stages of postnatal ontogeny: Concentrations of fluid and electrolytes in tissues.
In: Gazenko OG (editor).
Ontogenez mlekopitayushchikh v nevesomosti ***[Ontogeny of mammals in weightlessness.]***
Moscow: Nauka: 1988. Pages 120-122

Developmental Biology, Postnatal Ontogeny; Body Fluids, Fluid-Electrolyte Concentration
Rats, Neonates
Space Flight, COSMOS-1514

Abstract: On days 15 and 30 of the lives of rats exposed to space during days 13-18 of prenatal development, concentrations of fluid, potassium, sodium, calcium, and magnesium were measured in various tissues of experimental and control animals: in the bone (tibia), skin, liver, and kidney. Tissue was weighed and dehydrated to constant weight to determine concentration of water and dry substance. Then samples were placed in quartz test tubes containing concentrated nitric acid and placed in a dry-air bath at 80° until complete dissolution of organic substance. Next the acid was boiled off and samples were diluted with distilled water. Amounts of sodium and potassium were measured using flame photometry in an air-propane flame; and calcium and magnesium were measured in an air-acetylene flame on an atom adsorption spectrophotometer.

On day 15 of postnatal development, no reliable differences were found between the flight and control groups in kidney weight, amount of fluid, or concentrations of electrolytes. An analogous pattern was observed in studies of the liver, skin and bone tissue (Table 38). (Effects on magnesium in kidney are shown in the table, but not discussed.) Before day 15, the rats were nourished only on their mothers' milk; for this reason the fluid-electrolyte composition of their tissues was influenced by the mineral composition of the milk, which in turn depended on the mineral levels in the mothers' bodies. The fact that 15-day-old rats that had spent part of their intrauterine development in weightlessness displayed no significant aberrations in tissue mineral homeostasis, attests not only to its normal development and regulation in the offspring, but also to a definite degree of normalization of deviations noted in the females immediately postflight. No significant group differences were found on day 30 in any parameters studied.

Table 38: . Concentration of fluid and electrolytes in tissues.

Age	Grp	H_2O, kg/kg dry wgt	Na	K	Ca	Mg
			mequiv/kg dry wgt			
			Skin			
15	F	2.52±0.26	228.1±24.9	197.5±16.8	18.6±1.8	43.2±3.0
	SC	2.51±0.18	233.1±14.2	227.8±10.7	15.2±1.8	57.6±6.1
	VC	2.04±0.20	164.7±5.6	183.0±14.8	12.7±2.0	44.4±3.3
30	F	2.34±0.06	209.7±11.2	178.2±15.0	17.5±1.6	43.1±4.5
	SC	2.31±0.14	208.9±10.5	189.6±19.2	13.1±0.9	40.2±2.1
	VC	2.15±0.17	197.5±19.6	177.9±9.7	11.1±1.1	38.9±1.6
			Bone			
15	F	1.72±0.17	1731±124	185.6±23.7	18107±257	655.9±69.5
	SC	1.48±0.16	1837±116	167.4±20.9	15334±936	938.2±43.3
	VC	1.57±0.07	1913±141	160.3±10.7	15207±784	746.6±43.3
30	F	0.52±0.04	1444±240	73.4±5.4	10235±952	542±28
	SC	0.70±0.05	1427±46	80.7±10.9	12075±699	493±32
	VC	0.68±0.03	1331±28	84.3±7.7	10575±473	466±21
			Liver			
15	F	4.40±0.28	191.8±13.6	451.8±23.4	15.3±3.6	104.9±4.5
	SC	3.44±0.23	142.4±9.2	418.7±19.6	9.8±0.4	101.4±5.2
	VC	4.08±0.20	207.2±11.4	473.7±46.3	15.9±3.3	116.3±7.6
30	F	3.16±0.11	137.5±9.2	384.4±10.9	6.7±1.3	95.3±5.1
	SC	2.88±0.12	120.8±5.6	363.9±20.0	8.3±1.4	79.5±2.6
	VC	3.09±0.05	130.1±4.3	373.7±15.5	4.75±0.18	93.7±3.5
			Kidney			
Neonates	F	6.87±0.18	559.6±12.2 $p_s<0.01$ $p_v<0.02$	578.2±31.6	30.2±4.0	137.8±3.7 $p_s<0.001$ $p_v<0.05$
	SC	7.40±0.27	635±17.7	679.7±24	81.2±7.7	170.8±3.7
	VC	6.89±0.16	615.7±15.8	594.4±10.1	38.8±4.0	150.3±4.9
15	F	4.99±0.05	427.6±14.5	488.3±9.8	19.6±4.2	115.1±1.9 $p_v<0.05$
	SC	4.69±0.08	386.7±7.6	491.2±8.6	19.3±2.9	111.2±1.0 $p_v<0.05$
	VC	5.24±0.32	458.4±29.2	536.6±34.6	28.8 (n=2)	130.3±6.2
30	F	3.53±0.06	336.0±12.3	393.5±8.2	22.3±2.5	98.8±4.2
	SC	3.44±0.05	307.7±7.3	382.8±14.5	20.6±1.8	96.6±2.8
	VC	3.62±0.09	324.4±16.2	357.0±4.5	21.1±2.0	94.0±1.7

P1010(22/89) Luderits P, Markvardt D, Wachtel E (GDR), Belakovskiy MS (USSR), Hecht K, Grosser I (GDR)
Structure and metabolism of the organs of animals at various stages of postnatal ontogeny: Concentration of electrolytes in the coats and tails of the animals.
In: Gazenko OG (editor). Ontogenez mlekopitayushchikh v nevesomosti ***[Ontogeny of mammals in weightlessness.]***
Moscow: Nauka: 1988. Pages 122

Developmental Biology, Postnatal Ontogeny; Body Fluids, Electrolytes, Coats, Tails
Rats, Neonates
Space Flight, COSMOS-1514

Abstract: On days 15, 30, and 100 of the lives of animals exposed to space on days 13-18 of prenatal development and appropriate controls, the levels of potassium, sodium, calcium, magnesium, strontium, iron, phosphorus, zinc, copper, and manganese were measured in coat and tail tissue using at atom emission spectrometer. Samples of skin were taken from the backs (0.2-0.3 g) and ends of the tails (ca. 1.5 g). The coats of 15-day-old rats developing under space flight conditions displayed a significant elevation in the level of iron compared with the animals of both control groups. The levels of other mineral elements were the same as in the vivarium control. The tail tissues of 15-day-old flight rats showed a reliable decrease in levels of potassium, sodium, and iron, compared with the vivarium and synchronous control groups. No intergroup differences were found in 30- and 100-day-old animals.

P1111(22/89) Allers I, Allersova E (Czechoslovakia), Serova LV (USSR), Toropila MT (Czechoslovakia).
Structure and metabolism of the organs of animals at various stages of postnatal ontogeny: Lipid metabolism.
In: Gazenko OG (editor).
Ontogenez mlekopitayushchikh v nevesomosti ***[Ontogeny of mammals in weightlessness.]***
Moscow: Nauka: 1988. Pages 122-123.

Developmental Biology, Postnatal Ontogeny; Metabolism, Lipids
Rats, Neonates
Space Flight, COSMOS-1514

Abstract: The status of tissue lipids was assessed at various stages of postnatal ontogeny of animals developing after intrauterine exposure to weightlessness and corresponding controls. Methods used are not described. On days 15, 30, and 100, no intergroup differences were noted in concentration (with respect to organ weight) and absolute amount of triglycerides (Figure 45), phospholipids or cholesterol in the liver. In the thymus, triglyceride levels were significantly elevated in animals of the synchronous control group on day 30. No differences were noted between experimental and vivarium rats. Level of nonesterified fatty acids in the white fatty tissue of the animals developing in weightlessness was identical to that of the vivarium control on days 15, 30, and 100 of their lives; in the synchronous control group, the amount of nonesterified fatty acids was elevated in white fat on days 15 and 30.

The level of nonesterified fatty acid was elevated in the brown fat of the flight group compared to the vivarium control ($p<0.05$). On day 15, however, this parameter was even higher in the synchronous control animals and the difference between this latter group and the flight groups was not significant. On day 30 the concentration of nonesterified fatty acids was identical in the brown fat of animals of all three groups (figure 45).

The authors conclude that despite pronounced changes in lipid metabolism in female rats exposed to weightlessness while pregnant, lipid metabolism of their offspring was virtually unaltered compared to controls at various stages of postnatal ontogeny.

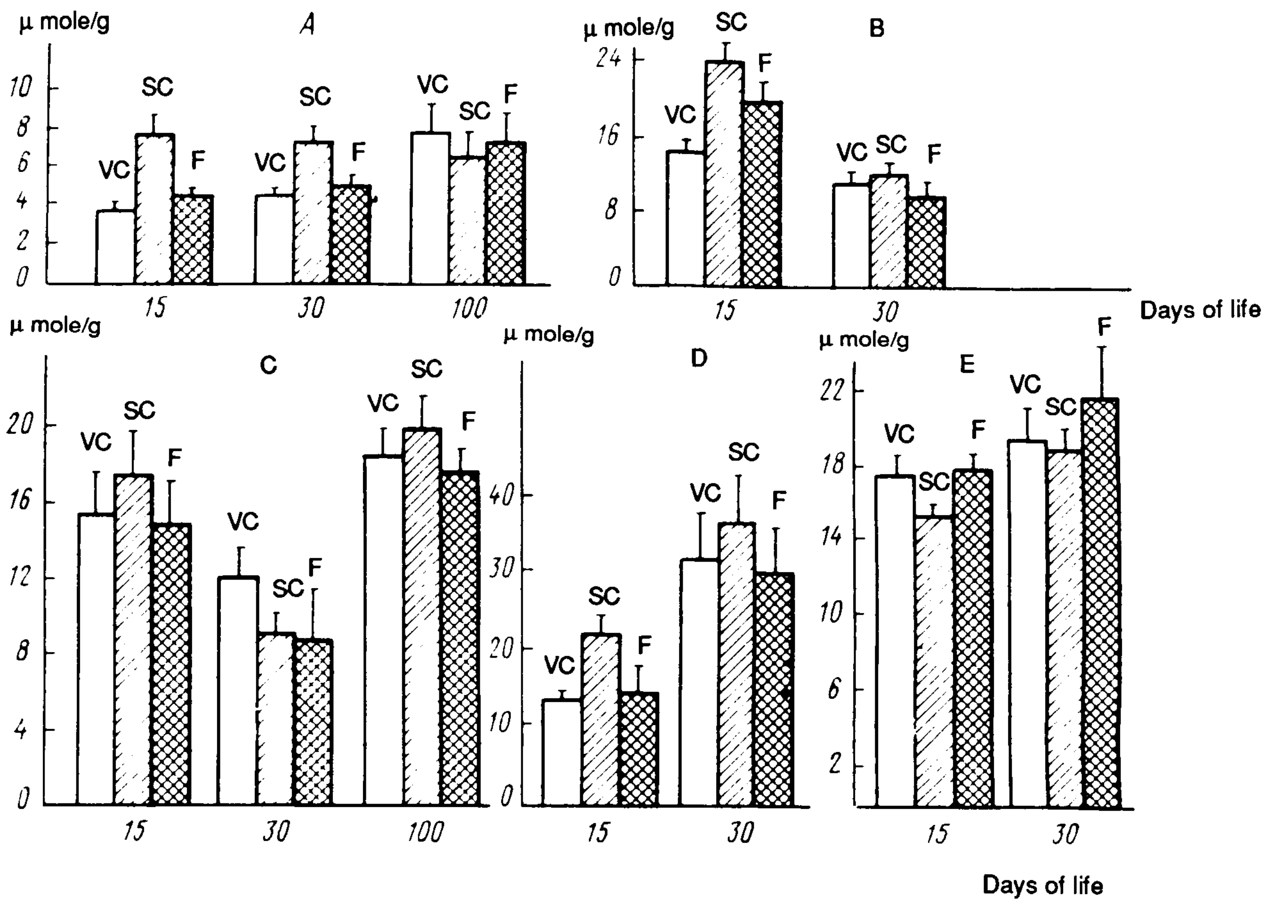


Figure 45: Postnatal ontogeny. Concentration on nonesterified fatty acids in white (A) and brown (B) fat tissue: Triglycerides in the liver (C) and thymus (D) and phospholipids in the thymus (E)

P1012(22/89) Mishurova E, Gabor Ya, Kropachova K (Czechoslovakia)
Structure and metabolism of the organs of animals at various stages of postnatal ontogeny: Concentration of nucleic acids in tissues.
In: Gazenko OG (editor).Ontogenez mlekopitayushchikh v nevesomosti ***[Ontogeny of mammals in weightlessness.]***
Moscow: Nauka: 1988. Pages 123-125.

Developmental Biology, Postnatal Ontogeny; Genetics, Nucleic Acids
Rats, Neonates
Space Flight, COSMOS-1514

Abstract Concentrations of nucleic acids in the liver, thymus and spleen were measured in rats exposed to weightlessness during days 13-18 of postnatal ontogeny and appropriate controls. A modification of a method used by Tsanev and Markov (not described) was employed, as well as methods estimating decay of DNA on the basis of level of polydeoxyribonucleotides. In 15-day-old flight and synchronous rats RNA tended to be depressed in liver tissue compared with the vivarium control group. No reliable differences were observed between the experimental flight group and the control groups in level of DNA in liver tissue.

Level of nucleic acids in thymus tissue was measured on days 30 and 100 of the animals' lives. No intergroup differences were found in absolute or relative levels of RNA or in DNA concentrations per gram (Table 40). On day 100, DNA concentration per organ was significantly higher in the thymus of vivarium control animals than in the synchronous group, but neither of these differed from flight animals. No intergroup differences were noted in the spleens of animals on day 100 in any parameter.

Table 39: Postnatal ontogeny. Concentration of nucleic acids in the liver

Parameter	**Group**	**Age, days** 15	30		100
RNA, mg/g	F	9.4±1.2	10.2±0.5	(ps<0.05)	6.0±0.4
	SC	10.6±0.9	7.5±0.7	(pv<0.05)	5.9±0.2
	VC	14.8±2.9	10.9±1.0		7.7±1.6
RNA, mg/organ	F	8.7±0.7	51.8±9.9		75.3±7.1
	SC	10.2±0.8	36.1±4.4	(pv<0.05)	74.4±6.5
	VC	14.0±2.1	53.8±5.0		101.1±23.0
DNA, mg/g	F	5.2±0.3	2.7±0.1		2.6±0.1
	SC	4.3±0.4	2.6±0.1		2.7±0.1
	VC	4.9±0.4	3.0±0.2		3.0±0.1
DNA, mg/organ	F	4.9±0.4	13.3±1.9		32.9±1.2
	SC	4.3±0.3	12.7±0.8		33.4±1.6
	VC	4.8±0.4	14.3±0.6		38.9±2.6

Table 40: Postnatal ontogeny. Concentration of nucleic acids in the thymus.

Parameter	**Group**	**Age, days** 30	100	
RNA, mg/g	F	22.1±2.7	18.6±1.4	
	SC	18.6±0.7	18.4±1.7	
	VC	20.0±3.3	22.7±3.5	
RNA, mg/organ	F	9.1±0.3	6.8±0.8	
	SC	8.5±0.7	6.9±0.7	
	VC	7.0±0.9	10.0±1.3	
DNA, mg/g	F	18.6±2.5	33.2±2.9	
	SC	19.3±0.6	29.8±2.3	
	VC	21.1±1.1	30.5±4.6	
DNA, mg/organ	F	7.8±1.1	12.3±1.2	
	SC	8.9±0.5	11.2±0.9	(pv<0.05)
	VC	7.3±0.2	16.5±2.1	

Table 41: Concentration of nucleic acids in the spleens of rats on day 100

Group	**RNA**		**DNA**	
	mg/g	mg/organ	mg/g	mg/organ
F	8.5±0.5	13.1±1.1	11.8±0.8	19.3±1.4
SC	11.4±4.1	15.9±6.0	16.9±5.2	23.7±4.7
VC	10.7±3.0	16.6±2.1	14.7±3.8	22.9±2.4

P1013(22/89) Makeyeva VF, Komolova IA, Yegorov IA (USSR)
Structure and metabolism of the organs of animals at various stages of postnatal ontogeny: Biosynthesis of nucleic acids.
In: Gazenko OG (editor).Ontogenez mlekopitayushchikh v nevesomosti ***[Ontogeny of mammals in weightlessness.]***
Moscow: Nauka: 1988. Pages 125-127.

Developmental Biology, Postnatal Ontogeny, Genetics, Nucleic Acids, Biosynthesis
Rats, Neonates
Space Flight, COSMOS-1514

Abstract: Rate of RNA synthesis in cell nuclei of the liver (on day 18 of prenatal development, and days 1, 15, 30, and 100 of postnatal development) and the rate of inclusion of radioactive precursors of DNA and RNA in lymphocytes of the spleen were measured in rats spending days 13-18 of prenatal ontogeny in space, and in appropriate controls. To study RNA-synthesizing activity, a nucleus was isolated from liver tissue in a solution of dense sucrose. A portion of the nucleus was used to determine transcription and from the remainder RNA-polymerase enzymes were obtained. Activity of the enzymes and RNA synthesis in the nuclei were estimated from the amount of radioactive precursor ^{3}H=UMP in acid-insoluble products of the RNA-polymerase reaction. Rate of biosynthesis of DNA and RNA in spleen lymphocytes were determined from amount of radioactive precursors *in situ*. Amounts of nucleic acids were measured spectrophotometrically.

Figure 46 presents results on the endogenous synthesis of RNA in the nuclei of hepatocytes in experimental and control animals. Elevations in flight rats on days 30 and 100 were significant. Analogous results were obtained when the activity of RNA-polymerases solubilized from nuclei of the liver was measured. In 30-day-old flight rats there was a 62% increase in enzyme activity compared with the synchronous and vivarium controls ($p<0.05$), while there was a 65% increase at 100 days ($p<0.05$).

The system used to determine enzyme activity involves the simultaneous function of RNA-polymerase I and RNA-polymerase II, synthesized from the precursors of rRNA and mRNA, respectively. The use of alpha amenitine, a specific inhibitor of RNA-polymerase II, made it possible to identify the contribution made by each form of the enzyme. It was demonstrated that when alpha-amenitine was added to the incubation medium (5 µg/ml), activity of RNA-polymerases in the liver cells of flight animals remained higher than in the vivarium and synchronous controls ($p<0.5$), supporting the conclusion that the elevated enzyme activity in the experimental rats was due both to RNA-polymerase I and RNA polymerase II.

Table 42 presents data on the rate of inclusion of radioactive precursors in nucleic acids of spleen lymphocytes in 30- and 100-day-old rats. No intergroup differences were found in DNA. However, the presence of the label in RNA in 100-day-old animals of the flight group was reliably depressed compared with the vivarium control. The synchronous group displayed a similar decrease.

The data obtained demonstrate that animals spending a portion of the prenatal period under conditions of space flight do not display any serious changes in anabolic metabolism of nucleic acids during postnatal ontogeny. However, it was true that transcriptional activity in liver cells was elevated in 30- and 100-day-old animals of the flight group.

Table 42 Postnatal ontogeny. Rate of inclusion of radioactive precursors in DNA and RNA in spleen lymphocytes

Age, days	Group	^{3}H-thymidine imp/min/µg DNA	^{14}C-uridine: imp/min/µg RNA
30	VC	133.6±4.1	11.0±1.1
	SC	149.9±13.9`	8.8±0.5
	F	135.9±11.3	11.1±0.7
100	VC	137.5±2.4	14.8±0.3
	SC	139.1±5.2	12.1±1.0
	F	137.8±4.9	10.7±0.6

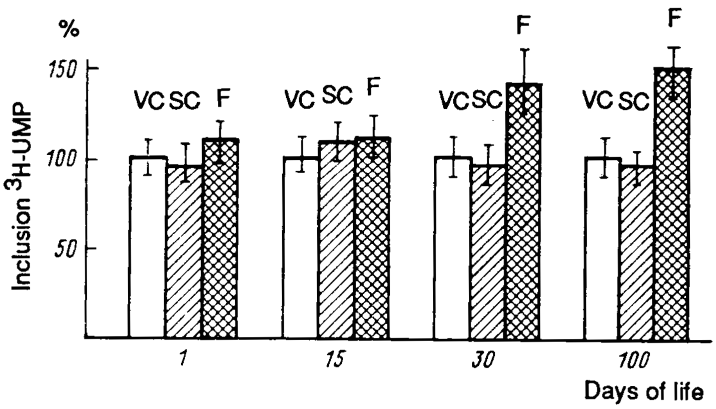


Figure 46: Postnatal ontogeny. RNA-synthesizing activity in the liver

P1014(22/89) Nemet Sh(Czechoslovakia)
Structure and metabolism of the organs of animals at various stages of postnatal ontogeny: Activity of certain enzymes in the liver.
In: Gazenko OG (editor). Ontogenez mlekopitayushchikh v nevesomosti ***[Ontogeny of mammals in weightlessness.]***
Moscow: Nauka: 1988. Pages 127-128.

Developmental Biology, Postnatal Ontogeny; Enzymology, Liver
Rats, Neonates
Space Flight, COSMOS-1514

Abstract: The activity of tyrosine-aminotransferase (TAT) and aspartate aminotransferase (AST) was measured in the livers of rats exposed prenatally (days 13-18) to weightlessness and in appropriate controls on days 15, 30, and 100 of the animals' lives. Activity of tryptophan-pyrolase (TP) and alanine-aminotransferase (ALT) were studied on days 30 and 100. Methods used are cited, but not described.

On day 15 of their lives, activity of TAT was reliably elevated in flight rats compared to corresponding parameters in the vivarium control; however, similar and even more marked changes occurred in the synchronous control group (Table 43). AST activity in the liver of flight rats was reliably below that in the vivarium control at this same time; however, decreased activity of this enzyme was also noted in the synchronous control group.

On day 30 there were no reliable differences between the experimental animals developing under conditions of weightlessness and the control animals in activity of TP, ALT, or AST in liver tissue. TAT activity was lower in flight animals than in the vivarium control, but did not differ from the synchronous control (Table 43).

On day 100, the activity of ALT and AST in the liver was analogous in the flight and control groups. TP activity was reliably higher in the flight animals than in the vivarium control, but did not differ from the synchronous control. TAT activity was elevated compared to the vivarium and synchronous control, but significantly so only in the former case.

Thus exposure to weightlessness during pregnancy not only failed to produce serious changes in the activity of TP and transaminases in the liver of female rats, but also failed to do so in their offspring at various stages of postnatal ontogeny.

Table 43: Postnatal ontogeny. Activity of liver enzymes

Parameter	Group	Age, days 15	30	100
TAT, mmole/g/min	F	18.5±4.0	7.8±0.8 (pv,0.01)	14.8±3.8
	SC	26.0±2.1 (pv<0.001)	8.5±1.8 (pv<0.05)	8.8±3.6
	VC	9.7±2.9	23.8±4,5	9.5±1.5
TP, mmole/g/hr	F	—	16.7±4.5	12.8±3.6
	SC	—	12.3±5.2	10.9±3.6
	VC	—	11.3±2.4	5.9±1.5
ALT, mmole/g/min	F	—	29.9±11.9	57.3±6.6
	SC	—	29.8±12.6	67.1±10.8
	VC	—	35.8±10.5	50.6±12.8
AST, mmole/g/min	F	234±49 (pv<0.05)	382±120	182±29
	SC	289±22	329±73	176±27
	VC	399±55	278±29	196±30

Note: Not all differences which appear to be significant are so marked

P1015(22/89) Pshchadal B, Peloukh V, Kolar F, Richter E, Dragota Z (Czechoslovakia)
Structure and metabolism of the organs of animals at various stages of postnatal ontogeny: State of the myocardium
In: Gazenko OG (editor). Ontogenez mlekopitayushchikh v nevesomosti ***[Ontogeny of mammals in weightlessness.]***
Moscow: Nauka: 1988. Pages 128.

Developmental Biology, Postnatal Ontogeny; Cardiovascular and Respiratory Systems, Myocardium
Rats, Neonates
Space Flight, COSMOS-1514

Abstract: The myocardium was studied in rats exposed to weightlessness during days 13-18 of prenatal ontogeny and in appropriate control animals on days 15, 30, and 100 of their lives. Absolute and relative myocardial weights were identical for animals of the experimental and control groups. No reliable differences were found between groups when the right and left cardiac ventricle and septum were weighed separately.

Hydration of myocardial tissue in experimental animals was the same as that of the control group on days 30 and 100. In flight rats there was a tendency for concentration of protein to increase in the tissue of the myocardium compared to the vivarium control on day 30, but this difference was no longer apparent on day 100.

P1016(22/89) Pospishilova I, Pospishil M. (Czechoslovakia), Serova LV (USSR)
Structure and metabolism of the organs of animals at various stages of postnatal ontogeny: Collagen metabolism in skin and bone tissue.
In: Gazenko OG (editor). Ontogenez mlekopitayushchikh v nevesomosti ***[Ontogeny of mammals in weightlessness.]***
Moscow: Nauka: 1988. Pages 128-133.

Developmental Biology, Postnatal Ontogeny; Musculoskeletal System, Collagen
Rats, Neonates
Space Flight, COSMOS-1514

Abstract: The goal of this work was to assess the possibility of changes in the postnatal development of certain organic components of connective tissue of the bones and skin in animals spending a portion of the prenatal period under space flight conditions. Attention was focused on the differences in the so-called genetic type of collagen, identifiable in the soluble fraction of collagen released by pepsin. Tissue samples (femur, skin of the back) from animals in the flight, synchronous, and vivarium control groups were analyzed immediately after birth and subsequently on days 15, 30, and 100 of the rats' lives. Skin (without fur) was taken from the animals back; the femur was cleaned of bone marrow. Samples of skin were frozen in liquid nitrogen and mechanically homogenized, solubilized, and then processed using zone precipitation chromatography. Hydroxyproline was measured at individual chromatogram peaks, and total protein was measured at the glycoprotein peaks. Total amount of insoluble collagen obtained using ultracentrifugation during the solubilization of samples was estimated on the basis of the quantity of hydroxyproline and used to compute the percentage of soluble collagen. Soluble collagen was measured in bone samples in the same way as in skin. Insoluble collagen was processed with cyanogen bromide, which split the collagen proteins into peptides specific to collagen I and III. These peptides were separated into ionexes? with a system of "rapid liquid chromatography," and their molecular weight was measured using permeation chromatography under pressure. The ratios among the different types of collagen were estimated on the basis of the ratios among peptides differing in molecular weight.

Due to low weight of bones in neonate rats and low collagen solubility in adult rats, tissue samples from individual animals had to be combined to obtain amounts sufficient for analysis. A total of 2-7 samples were combined to generate 1-2 values for each group, making statistical analysis impossible.

Figures 47 and 48 show that at all stages of postnatal ontogeny animals spending a portion of their prenatal development period under conditions of weightlessness displayed alterations in collagen metabolism in the skin and bone tissue compared with animals of the vivarium and synchronous control groups.

In the present experiment, the bone tissue of control animals revealed age-related changes in collagen metabolism, which can be considered a manifestation of maturity and stabilization of the ultrastructures: gradual decrease in concentration of soluble collagen, increase in the percentage of type Ia and Ib, and decrease in the levels of collagen II and III. The bone tissue of experimental animals exposed to space flight conditions during the prenatal period displayed deviations from normal age-related changes in collagen metabolism in bone, attesting to a delay in the development of the tissue and some degree of immaturity in mature animals, including higher solubility of collagen, a decrease in the ratio of hydroxyproline to glycoproteins, slower increases in type Ib collagen, and retention of higher concentrations of types II and III collagen in the soluble fraction.

Age-related changes in collagen metabolism in the skin of control animals were analogous to changes in bone for a number of parameters, while for other parameters changes were specific

to skin. In the experimental animals, both the rate of decrease in the proportion of soluble collagens and the rate of increase in the ratio of hydroxyproline to glycoproteins grew slower as animals matured. There were a number of intergroup differences (e.g., increase in type III collagen in the flight group) indicative of abnormal development and greater immaturity in the flight group at all the ages studied

The reasons for the changes described are as yet unclear. The occurrence of the same type of changes in the metabolism of connective tissue in skin and bone of experimental animals suggests that these changes are systemic in nature.

It is possible that the reason for the differences found here between experimental and control animals was a change in the hormonal status of the mothers, due to exposure to weightlessness during pregnancy.

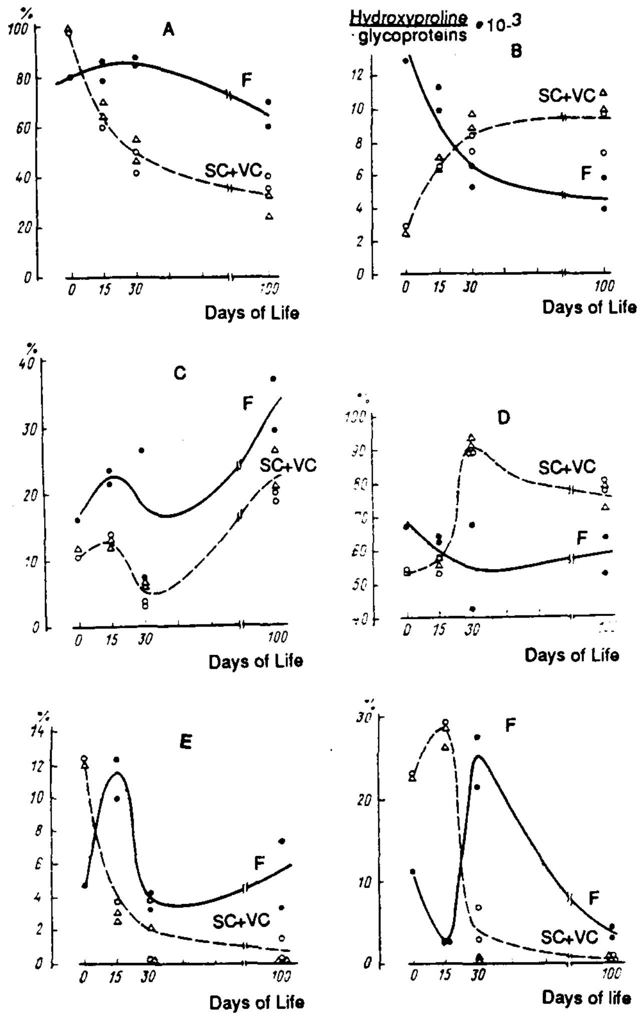


Figure 47: Postnatal ontogeny. Collagen metabolism in bone tissue. Soluble collagen (A), ratio of hydroxyproline to glycoproteins (B), type Ia collagen (C), type Ib collagen (D), type II collagen (E), type III collagen (F).

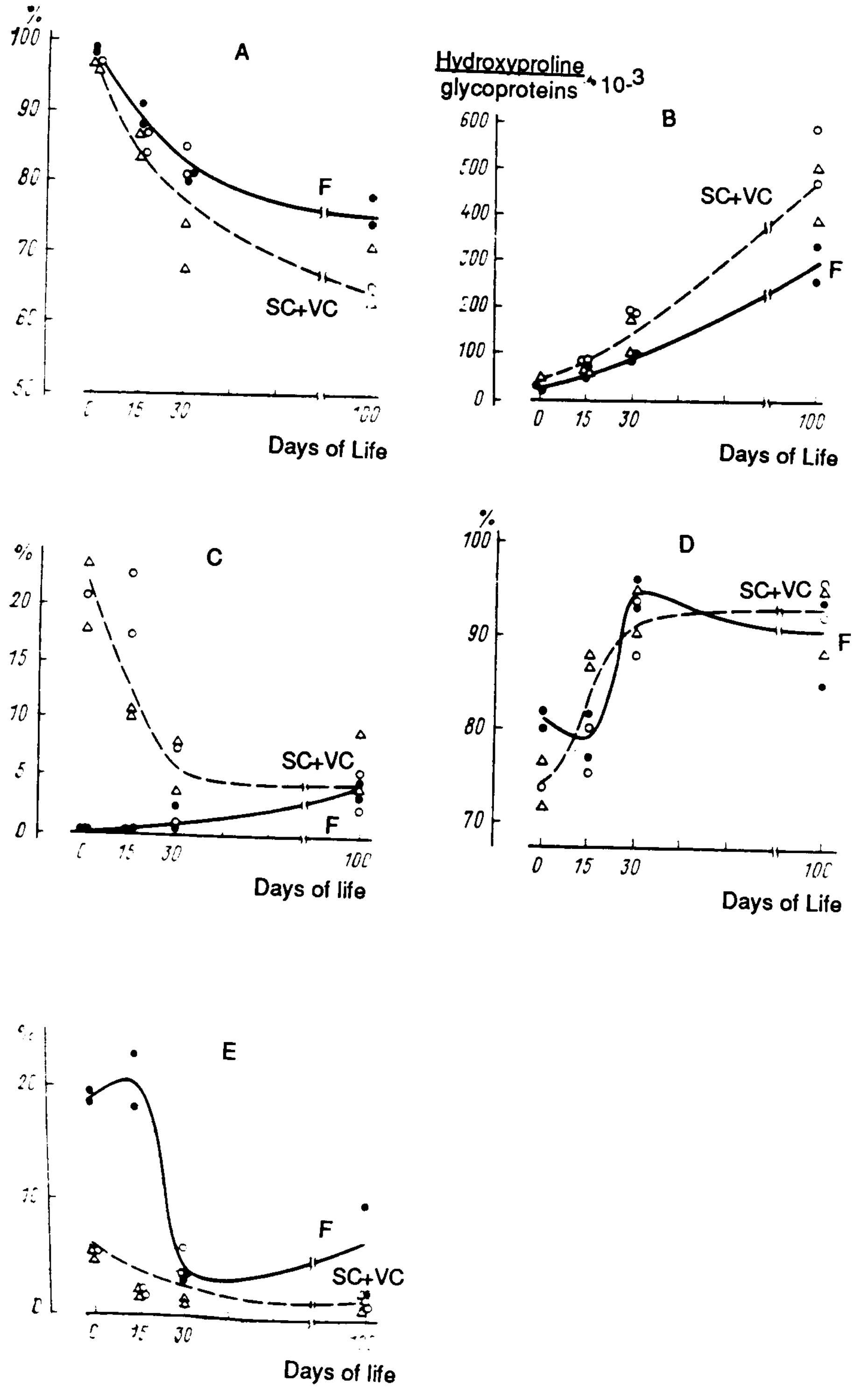


Figure 48. Postnatal ontogeny. Collagen metabolism in skin. Soluble collagen (A), ratio of hydroxyproline to glycoproteins (B), type Ia collagen (C), type Ib collagen (D), type II collagen (E), type III collagen (F).

P1017(22/89) Shappar D, Alexander K, Laboreau JC, Lora B, Robert JM, Riffa G (France)
Structure and metabolism of the organs of animals at various stages of postnatal ontogeny: Structure of cartilage.
In: Gazenko OG (editor). Ontogenez mlekopitayushchikh v nevesomosti ***[Ontogeny of mammals in weightlessness.]***
Moscow: Nauka: 1988. Pages 133-134.

Developmental Biology, Postnatal Ontogeny; Musculoskeletal System, Cartilage
Rats, Neonates
Space Flight, COSMOS-1514

Abstract: A scanning electron microscope was used to study the structure of cartilage tissue in the area of the proximal epiphysis of the tibia in animals developing in weightlessness and in control animals, on days 15, 30, and 100 of postnatal ontogeny. The material was fixed in formalin and processed using methods described by A. Boyde (1972). The techniques used provided a qualitative description of the loci of primary cartilage mineralization, the so-called calcified globules or calcospherites.

Normally, growth cartilage has three differentiated zones, representing three types of tissue: the cartilaginous zone, consisting of several layers (reserve, proliferating, hypertrophying, and calcifying); the bone zone, starting in the foundation of the cartilaginous calcifying columns; and the fibrous peripheral zone. Because cartilage normally has a high rate of metabolism, the formation of bone tissue is proportional to growth of the organism

When material was observed with low magnification, which shows the various layers of cartilaginous zones and their orientation well, no reliable differences were found at various stages of postnatal development between the experimental animals, developing in weightlessness, and the controls. Nor were differences found in the hypertrophying layer or the proliferating layer at any observation point.

The results obtained support a conclusion that postnatal cartilage mineralization and differentiation of bone tissue in rats spending a portion of the prenatal development period exposed to weightlessness are virtually identical to those processes in the norm.

P1018(22/89) Benova DK(Bulgaria)
Structure and metabolism of the organs of animals at various stages of postnatal ontogeny: Cytogenetic study of sex cells.
In: Gazenko OG (editor). Ontogenez mlekopitayushchikh v nevesomosti ***[Ontogeny of mammals in weightlessness.]***
Moscow: Nauka: 1988. Pages 134-135.

Developmental Biology, Postnatal Ontogeny; Reproductive System, Genetics, Cytology, Spermatocytes, Translocations
Rats, Neonates
Space Flight, COSMOS-1514

Abstract: When male rats exposed to weightlessness during prenatal development reached the age of 100 days, a cytological investigation of their sex cells was conducted. Results were compared to sex cells in control animals. Preparations were made from the testes using a modification of a method introduced by A. P. Dyban. A total of 12 rats were examined: 4 each of the flight, and vivarium and synchronous control groups. For each animal, a total of 200 spermatocytes in the metaphase were studied. The numbers of reciprocal translocations in the form of multivalent rings and chains were counted. At this stage of spermatogenesis in rats, 21 pairs of chromosomes (bivalents) are formed. Because the complexity of the configuration makes analysis difficult, all preparations were analyzed by three additional experts. An analysis of variance was conducted.

In animals of the flight group a total of 815 cells from 4 animals were analyzed. A total of 7 cells (0.9%) were found with translocations; no translocations were found in analysis of 803 cells from the vivarium control groups ($p<0.001$). However, the increase in the number of translocations was also observed in the synchronous control group (0.5%). The differences between the flight and synchronous control groups were not statistically significant ($p<0.005$), supporting attribution of the changes found not to weightlessness, but to concomitant space flight factors (vibration, acceleration, etc.), which were simulated in the synchronous control group. At the same time, the results do not preclude the possibility of a mutagenic effect of weightlessness on the germ cells of mammalian fetuses. It should be noted that from the moment of exposure to weightlessness (days 13-18 of prenatal ontogeny) to the moment the anomalies were discovered (100 days of life), the cells studied completed a large number of cell divisions and stages of differentiation, during which the anomalous cells could have been "weeded out." Moreover, although the difference between the flight group and the ground-based synchronous control was not significant the number of cells with translocations was half the size in the latter case (0.9 and 0.5%, respectively), and translocations were found in only two of the four animals, while in the flight group translocations were present in all animals studied.

ENZYMOLOGY

PAPERS:

P984(22/89)* Vetrova YeG, Krasnov IB.
Activity of dehydrogenase in the liver of rats after 30-days of exposure to hypergravity.
Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.
22(6): 64-66; 1988.
(9 references; 3 in English)

Enzymology, Liver Dehydrogenase Activity
Rats
Gravitational Biology, Hypergravity, Centrifugation

Anstract: This study was undertaken to investigate the activity of NAD-dependent malate dehydrogenase (MDH) and NADP-dependent isocitrate dehydrogenases (ISDH) in the mitochondria and MDH, ISDH, and lactate dehydrogenase (LDH) in the cytoplasmic fraction of hematocytes in the livers of rats after 30 days of exposure to increased gravity of levels 1.1 and 2 g and also 2 and 7 days after termination of this treatment. Increased gravity was achieved by rotating rats in chambers either central or peripheral to the arms of a centrifuge. On day 30 of this treatment and days 2 and 7 post-treatment, the animals in the 1.1 and 2 g groups, along with a vivarium control, were decapitated. Mitochondrial and cytoplasmic fractions of hematocytes were isolated from a 25% homogenate of the liver, prepared in a 0.25 M solution of sucrose in 0.03 M tris-HCl-buffer with pH of 7.8, 0.025 M KCl and 0.05 $Mg(CH_3COO)_2$. The homogenate was centrifuged for 10 minutes at 800 g; the sedimentation nucleus was discarded and the supernatant centrifuged for 15 minutes at 11,000 g. The mitochondrial precipitate was resuspended in 0.03 M solution of sucrose and again centrifuged. The resulting sedimentation was resuspended in a 0.5 ml solution of sucrose and the first supernatant, the cytoplasmic fraction, was frozen. The mitochondrial fraction was subjected to 1.5 hours of dialysis against a 0.01 M tris-HCl-buffer with pH of 7.6 to produce a matrix, and the cytoplasmic fraction was used to determine enzyme activity spectrophotometrically. Protein concentration was measured using a method developed by Lowry. Student's t for small samples was used to test for statistical significance. Comparative data are provided from an earlier study in which rats underwent 70 days of hypokinesia.

On day 30 of centrifugation, activity of mitochondrial MDH and ISDH in hepatocytes was significantly depressed in both experimental groups, with no difference between them. Activity of cytoplasmic MDH and ISDH was depressed only in the 2-g group. Cytoplasmic ISDH and LDH activity was not affected by the treatment. Since similar results occur under weightlessness and hypokinesia, the authors attribute the effect to reduced motor activity in both conditions. On day 2 after recovery, cytoplasmic enzyme activity was restored to normal for the 2-g group and mitochondrial ISCH activity was normalized for both groups. Activity of mitochondrial MDH remained depressed in both groups. On day 7 after treatment termination, mitochondrial MDH had normalized, but for both groups mitochondrial ICDH activity was above that of the control group, suggesting intensified biosynthetic processes.

Table 1: Activity of MDH, ISDH, and LDH in mitochondria and cytoplasmic fractions of liver hepatocytes of rats undergoing and recovering from hypergravity

Table 2: Activity of MDH and ISDH of mitochondrial and cytoplasmic hepatocytes of rats undergoing 70 days of hypokinesia

P996(22/89) Tverdokhlib VP, Konovalova GG, Lankin VZ, Meyerson FS.

The effects of adaptation to hypoxia on the activity of antioxidant enzymes in the liver of animals undergoing stress.

Byulleten' Eksperimental'noy Biologii i Meditsiny.
1988(11): 528-529.

Authors' Affiliation: All-Union Cardiological Research Center, USSR Academy of Medicine, Moscow; Institute of Pathology and Pathological Physiology; Orenburg Medical Institute

Enzymology, Anitoxidant Enzymes, Liver; Metabolism, Lipid Peroxidation
Rats
Psychology, Stress; Adaptation, Hypoxia

Abstract: Subjects in this experiment were male Wistar rats (n not specified). Experimental animals were exposed (duration of exposure not specified) to "emotional-pain stress" (a paradigm where an instrumental response, learned to avoid shock, ceases to be effective), and sacrificed either 2 or 24 hours after treatment termination. Half the experimental animals were preadapted periodically to hypoxia by exposure to a height equivalent of 5000 m in a barochamber for a 6-hour period 6 times a week over a period of 1.5 months. On the day after the final adaptation session, the animals were exposed to stress and then sacrificed after the specified intervals. Two control conditions were used, either untreated animals or animals exposed to hypoxia, but not to stress. The livers of the sacrificed animals were homogenized in a 50 mM phosphate buffer (pH 7.4) and centrifuged at 800 G for 10 minutes. Activity of antioxidant enzymes was measured in a supernatant solution. Activity of superoxide dismutase (SOD) was determined on the basis of inhibition of reduction of blue nitrotetrazole in a xanthine-xanthine oxidase system, while activity of glutathione peroxidase was established on the basis of oxidation of NADPH in a conjugate glutathione reductase system using tretbutyl hydroperoxide as a substrate. The activity of glutathione-S-transferase was determined on the basis of formation of glutathione with 1-chlorine-2,4-dinitrobenzole. Spectrophotometry was used. Concentration of malonic dialdehyde was measured in liver tissues on the basis of reactions with 2-thiobarbituric acid, and protein concentration was measured using the biuret reaction.

In animals exposed to stress, concentration of malonic dialdehyde (MDA) increased markedly in the liver 2 hours after exposure, but normalized after 24 hours. Another indicator that stress increased lipid peroxidation in the liver was the sharp decrease in SOD; however the activity of enzymes utilizing lipoperoxides, glutathione peroxidases, and glutathione-S-transferases was virtually unaffected after both time intervals. Exposure to hypoxia had no effect on liver MDA either in stressed or unstressed animals. SOD activity increased by almost 65% in animals adapted to hypoxia and decreased by no more than 27%, remaining above that of non-preadapted stress animals after stress. Activity of glutathione peroxidase decreased by almost a factor of 4 after hypoxia, but underwent no further changes attributable to stress. These data suggest that adaptation to hypoxia may prevent or attenuate liver damage due to stress.

Table: Concentration of MDA and activity of antioxidant enzymes in the livers of animals adapted and not adapted to hypoxia

P1036(22/89)* Drozdeva TY, Vetrova YeG, Popova IA, Korol'kov VI, Dotsenko MA, Gordeyev YuV.
The effects of vibration, impact, and radial acceleration on blood enzyme activity of primates.
Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.
23(1):86-89; 1989.
[8 references; 1 in English]

Enzymology, Blood Enzymes
Primates, Rhesus Monkeys, Males
Habitability and Environmental Effects, Vibration, Impact, Radial Acceleration

Abstract: Experiments were performed on 3-year-old male rhesus monkeys (not clear how many). Primates were exposed to vibration (ranging from 20 to 2500 Hz) in a standard primate chair for 10 minutes with linear changes in acceleration from 1- to 8-G in the horizontal position, and also while the animal in the chair was at an angle of 30° and 90° to the horizontal. Impact acceleration of 29- to 35-G was created on an impact testing stand by stopping a falling platform with a system of foam rubber slabs. Primates were secured on the platform in a contoured shock-absorbing couch at an angle of 30°. Radial acceleration ($+G_Z$) peaking to 8.2-G with rate of increase of 0.06 G/second was produced on a centrifuge. Blood was taken from veins of the lower limbs, 30 minutes before the treatment and 30 minutes after. Activity of the following enzymes was measured: alanine aminotransferase (ALT), aspartate aminotransferase (AST), isocitrate dehydrogenase (IDH), lactate dehydrogenase (LDH), malate dehydrogenase (MDH), and creatine phosphokinase (CPK) in serum using standard reagents. Distribution of CPK isoforms was further examined. Student's t was applied to results.

ALT, AST, and IDH activity was not altered by vibration, while activity of LDH, MDH, and CFK increased after vibration for all positions. MDH increased most at an angle of 30°, LDH at an angle of 90°, and CPK at an angle of 30°. Impact forces led to statistically significant increases in activity of MDH, CPK, LDH, and IDH. Radial acceleration led to significant increase in the activity of all the enzymes, with CPK, and IDH increasing by a factor of almost 7.

Table: Enzyme activity in the blood serum of primates

GENETICS

PAPER:

P993(22/89) Meyerson FZ, Fomin NA, Pavlova VI, Shibkova DZ.
Recovery of organ mass and nucleic acids after long-term hypokinesia.
Patologicheskaya Fiziologiya i Eksperimenta'naya Terapiya
1988(6): 59-63.
[8 references; 1 in English]
Authors' Affiliation: Laboratory of Cardiac Pathophysiology, Institute of General Pathology and Pathological Physiology, USSR Academy of Medicine, Moscow; Department of Physiology and Anatomy, Chelyabinsk Teachers College

Genetics, Nucleic Acids; Developmental Biology, Normal Growth, Body Weight
Rats
Hypokinesia, Long-Term; Immobilization; Recovery

Abstract: This study evaluated the pattern of changes in weight of the body and major organs and organ levels of nucleic acids during and after long-term hypokinesia. Subjects were 450 2-month-old male Wistar rats. Hypokinesia was induced by placing the animals in immobilization cages for 60 days. After this period, animals were placed in larger cages. On days 5, 10, 20, 30, and 60 of treatment and also on days 5, 10, 20 and 30 of recovery at least 10 animals were sacrificed. Animals of a matched control group were sacrificed at the same time. All the animals were weighed before sacrifice. When the organs were weighed it was assumed that the dry residue of tissues does not change during hypokinesia. Concentrations of DNA and RNA were determined spectrophotometrically in tissues of the brain, heart, liver, spleen, and thymus. Concentrations were expressed in mg per organ.

Although hypokinesia stopped normal growth in control animals completely, actual weight loss did not occur. After treatment termination, animals rapidly grew and gained weight, but were still 15% behind controls after 30 days. Changes in heart weight were similar to those in total weight, except that heart weight had normalized by 30 days post-treatment. The weight of the cerebrum continued to increase during hypokinesia, remaining slightly behind that of the control, but recovering fully by day 20 post-treatment. During hypokinesia, the weight of the gastrocnemius and liver actually decreased by 20-30%, and that of the thymus by 50%; during the recovery period, the weight of the thymus and liver reached control values, while that of the gastrocnemius was depressed by 20%. Thus, the rapid recovery of growth after hypokinesia seems to indicate that the neurohumoral and cellular components of the growth mechanisms are retained during hypokinesia and are reactivated as soon as the treatment is terminated. This would lead to the prediction that the number of genomes in an organ and thus the concentration of DNA remain relatively unaffected.

In control animals, it was evident that in all organs, except the thymus physiological growth is accompanied by increases in nucleic acids. Long-term hypokinesia had different effects on DNA and RNA in the organs. In the heart, DNA remained the same throughout the hypokinesia period, so that it was analogous in 4-month-old experimental rats to that of 2-month-old controls. During recovery cardiac DNA increased by 51% in 1 month and was the same as that of control animals of matched age. RNA in the heart decreased by 20% during treatment. Since DNA was unaltered, this would suggest decreased transcription rate. During the 1-month recovery period, RNA doubled in the heart. In the gastrocnemius, hypokinesia failed to completely inhibit DNA synthesis, but this process was retarded compared to control. After treatment, DNA level recovered rapidly. RNA concentration in this muscle remained unaltered throughout treatment, but subsequently increased to control level. In the liver, DNA decreased by 25% during hypokinesia, but had risen above control level after 1 month's recovery. Liver RNA also decreased and then recovered to control level. In the thymus of normal animals, nucleic acids

decreased with age due to involution; decreases were even more pronounced in the experimental animals immediately after treatment. After treatment terminated, the level of nucleic acids in the thymus recovered, exceeding those of controls of the same age. Normal increases in nucleic acids in the brain were only slightly inhibited by hypokinesia. Detailed analysis revealed slightly greater decreases in RNA than in DNA in the heart and skeletal muscles during hypokinesia; subsequent to it RNA increased more rapidly. This led to rapid changes in the RNA/DNA ratio after treatment termination.

The authors conclude that hypokinesia-inhibited growth of relatively young animals is reversible. However, it is possible that if hypokinesia were extended further in duration some changes might not be reversible.

Table: Concentration of nucleic acids in control rats at 2, 4, and 5 months; and in 4-month-old animals undergoing 2 months of hypokinesia; and 1 month after its cessation.

Figure 1: Changes in weight of body, heart, cerebrum, gastrocnemius muscle, liver, and thymus in response to 2-months of hypokinesiaand in normal animals

Figure 3: Change in the ratio of RNA/DNA in the heart, skeletal muscles, and liver in response to 2 months of hypokinesia and in control animals

GRAVITATIONAL BIOLOGY

PAPERS:

P1040(22/89) Gomazkov OA, Rostovtsev AP, Komissarova NV, Panfilov AD, Yelistatova IA, Fomin VV.
The activity of enkephalin- and angiotensin II-forming peptidases of the brain and peripheral tissues under conditions of chronic stress induced by hypergravity.
Patologicheskaya Fiziologiya i Eksperimental'naya Terapiya.
1988(5): 52-57
[28 references; 18 in English]
Authors' Affiliation: Institute of Medical Enzymology, USSR Academy of Medicine, Moscow.

Neurophysiology, Enzymology, Brain Peptidases, Enkephalin, Angiotensin, Endocrinology, Hypophysis, Adrenal Gland, Immunology
Rats, Male

Abstract: Subjects in this experiment were male Wistar rats exposed to hypergravity of 2 g by continual rotation on a centrifuge with radius of 1.41 m, at a rate of 33 revolutions per minute. The centrifuge was stopped for 30 minutes per day. After 1, 3, and 5 days, some of the animals were sacrificed. Animals of the experimental and control groups received mixed feed. The control animals were housed in the same room as the centrifuge. Activity of enkephalin-forming carboxypeptidase (EC.3.4.17.10), carboxypeptidase B, and angiotensin-converting enzyme (EC.3.4.15.21) were measured in the hypophysis, portions of the brain (hypothalamus+thalamus, midbrain, striatum), and adrenal glands. Activity of angiotensin-converting enzyme (ACE) was further measured in the kidney and lung. Tissue was processed in the cold, and stored at -20° before measurement. Activity of enkephalin-forming carboxypepdidase (EFC) was measured using dansyl-fen-ala-arg as a substrate, while ACE activity was measured using kbz-fen-gis-leu. Immunological parameters (natural antibody and receptor protein) were measured in frozen blood serum warmed to 56°C.

After 1 day of rotation, natural antibodies and receptor proteins were elevated by factors of 3.7 and 13.5, respectively; these parameters continued to rise during the next 4 days, suggesting activation of catabolic processes typical of stress response. In the norm, EFC is highly active in the hypophysis and the striatum, and 30-100% less so in the remaining portions of the brain and the adrenal glands. After 1 day of centrifugation, EFC activity had decreased in the striatum, thalamus and hypothalamus area and hypophysis by 25, 13, and 18% respectively. On days 3-5 of the experiment, this parameter had returned to baseline. No changes were noted in enzyme activity of the midbrain. In the adrenal glands, EFC activity had decreased by 35% after 5 days. Changes in activity of carboxypeptidase in response to gravity stress were analogous to those in EFC in the thalamus and hypothalamus, hypophysis, and adrenal glands, although they differed in the striatum and midbrain [This statement does not appear to be corroborated in theFigure.] One possible explanation for depression of EFC activity in the brain and hypophysis during early exposure to hypergravity is inhibition by metabolites forming during this period. However, given the level of dilution used in the measurement procedure, it is unlikely that metabolites were present in sufficient quantities to cause the effects observed. The authors consider it more likely that a portion of the free EFC in the secretory granules of the hypophysis and chromaffin granules of the adrenals was emitted along with enkephalins into the extracellular space, where it was deactivated by proteases. Thus, decreased EFC activity during initial exposure to gravity could reflect loss of some enzyme molecules in the process of liberating enkephalins. Subsequently, compensatory processes would begin leading to restoration of EFC level. Recovery of EFC activity in the brain and its increase in the adrenals could occur either *de novo* or through conversion of some of the membrane-bound, less active forms into the free, more active form. In the norm, ACE activity is most pronounced in the lungs and higher for the

hypophysis than the other central tissue regions. Hypergravity was not associated with changes in ACE in the hypophysis, thalamus/hypothalamus, or lungs. In the striatum, kidneys, and adrenal glands, small decreases in ACE activity were noted on day 1, after which gradual increases to above initial level were noted. These facts suggest the stimulation of processes leading to formation of angiotensin II.

The authors argue that the changes in the activity of the angiotensin system in the brain and in the peripheral tissue may lead to various functional shifts in blood pressure, renal circulation, and consumption of liquids, all associated with adaptation to hypergravity. It can further be hypothesized that inhibition of ACE activity in the midbrain is one of the mechanisms for limiting pressor and diuretic central effects during gravitational stress.

Table: AC E in rats during exposure to hypergravity

Figure 1: Changes in levels of natural antibodies and receptor proteins during exposure to hypergravity

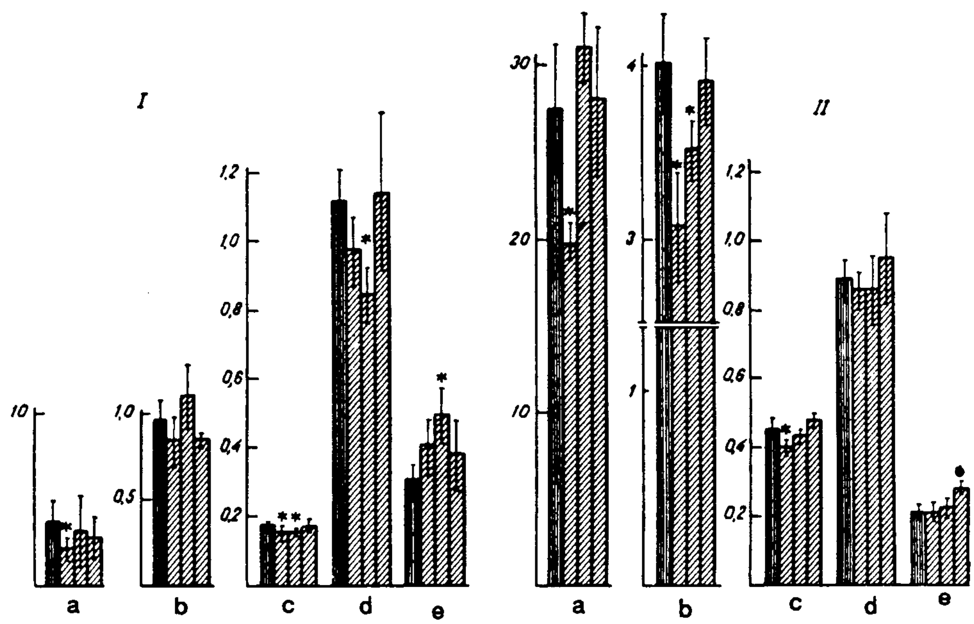


Figure 2: Changes in activity of carboxypeptidase (1) and enkephalin forming-carboxypeptidase (II) during exposure to hypergravity

a- hypophysis; b - striatum; c - thalamus-hypothalamus, d - adrenal glands. Ordinate - enzyme activity (in nmole dan-syl-phen-ala during 1 minute per 1 mg protein). Vertically hatched bars represent control group, diagonally hatched bars represent animals exposed to hypergravity at three intervals (days 1, 3, and 5); * statistically significant ($p<0.05$) with respect to control group

P1000(22/89) Serova LV, Denisova LA, Pustynnikova AM (U.S.S.R.).
A comparative analysis of the effects of weightlessness and hypergravity on the prenatal development of mammals.
In: Gazenko OG (editor). Ontogenez mlekopitayushchikh v nevesomosti ***[Ontogeny of mammals in weightlessness.]***
Moscow: Nauka: 1988. Pages 147-151.

Gravitational Biology, Developmental Biology, Prenatal Development, Reproductive System
Rats, Mice
Space Flight, COSMOS-1514; Hypergravity, Centrifugation

Abstract: A great deal of empirical material has been accumulated on the effects of hypergravity on living organisms. Experiments have been performed involving long-term (up to and exceeding a year) exposure of animals at various evolutionary levels to centrifugation at 2-7 g. It has been demonstrated that even at 7 g, mice survive for a year; whereas, at 2 g mice and rats have a normal life-span and are capable of conceiving and bearing young.

Experiments with mammals exposed to weightlessness are still of considerably shorter duration than those with hypergravity. No irreversible changes were found in the organs of rats exposed to weightlessness on COSMOS biosatellites for up to 22 days, (i.e. approximately 1/50th of their normal lifespans.) Still, this does not tell us how adaptation to weightlessness would proceed if the duration of exposure were increased.

It can be hypothesized that there are two ways in which altered gravitational force affects a living organism:

1. Specific (mechanical) effects associated with changes in the positions of organs and tissues relative to each other, and with individual components in cells and tissues, as well as with changes in energy expended to work against the force of gravity.

2. Nonspecific effects, such as a stress response.

It is obvious that the extent to which the specific effects of altered gravity manifest themselves depends on the size of the organism and is greater for larger animals; the magnitude of the nonspecific effects is determined by the level of organization of the neural and endocrine systems of the animals, i.e., the complexity of these systems, which is greater for higher animals.

Using these theoretical considerations as a basis, the authors used adult rats and mice in an attempt to compare the physiological effects of weightlessness and hypergravity of 2 g. They demonstrated that change in the level of gravitation within the limits $\pm$ 1 is accompanied by the development of a stress reaction manifested by a delay in growth and by involution of lymphoid organs, neutrophilia, and lymphopenia in the blood and other changes. Nonspecific changes develop along with specific changes in the musculoskeletal system, the myocardium, and the erythrocytic system. However, the proportion of the nonspecific component is substantial and could possibly represent the majority of functional and structural changes that occur under these conditions, including those usually considered specific.

An analogous pattern can be observed in the response of pregnant female rats to weightlessness and hypergravity. The authors go on to compare certain results of the embryological experiment performed under space flight conditions on the COSMOS-1514 biosatellite and a ground-based simulation experiment on the centrifuge preceding the flight. The experiment in weightlessness lasted 5 days (from days 13 to 18 of pregnancy), while the hypergravity experiment lasted 7 days (from day 14 to 21 of pregnancy). In both instances, the mother-fetus system was

exposed during the last third of pregnancy — at the stage of active growth of the fetus and development of organs. In both situations there were serious changes in the mother, as evidenced by retardation of weight increases amounting to 60-65 g, i.e., by virtually one quarter of the females' own weights.

Nevertheless, the parameters of reproductive function of the animals exposed to weightlessness and hypogravity were not altered: the number of implantation and resorption sites and the number of living fetuses were identical in the experimental and control conditions of both experiments. Fetal weights were depressed by 10-12% ($p<0.05$), while tissue hydration in fetuses developing in weightlessness was elevated by 6% ($p<0.05$). No analogous changes were noted in fetuses developing in hypergravity.

No differences were observed in the total concentration of calcium in fetuses developing in weightlessness and hypergravity compared to control animals; nevertheless, in both cases there was inhibition of skeletal development in the fetuses, as manifested by a reliable decrease in the dimensions of ossification sites in the bones of the extremities and axial skeleton.

There were also differences in the reactions of the mother-fetus system to weightlessness and hypergravity. For example, rats exposed to space during days 13 to 18 of pregnancy displayed a more than 50% decrease in concentration of calcium in liver and kidney tissue, while rats exposed to 2 g did not display such changes. Other differences were also identified between groups exposed to weightlessness and hypergravity. However, the authors argue that what is most important is that when gravity alters by 1 g "up" or "down" from Earth's gravity, i.e., change in opposite directions, the overall pattern of changes in the mother-fetus system is the same. Both cases engender serious changes in the mothers' bodies, similar to those in stress reactions; however, parameters of embryo death are unaltered, and the developing fetuses are only slightly behind the controls in body weight and dimension of ossification sites. The data obtained are analogous to results of previous experiments on mature rats and reveal the important contribution made by the nonspecific (stress) component in the reactions of mammals to the gravitational factor, when the force of gravity alters within limits of $\pm$ 1 g compared to that on Earth. The authors recommend that centrifugation of 2 g be used as a model within a future research program directed at studying the total cycle of prenatal development in mammals under space flight conditions. The authors conducted a series of experiments with rats on a centrifuge at 2 g, to test the possibility of impregnation and early prenatal development under these conditions.

Results showed that there are diverse mechanisms underlying the effects of hypergravity of 2 g at various stages of prenatal development of mammals. When animals were mated under conditions of 2 g the major difference from control was the increase in the time elapsed between the point the males and females were placed together and the time mating occurs. When rats were placed in a centrifuge starting on day 7 of pregnancy, i.e., during the implantation period, the major change compared to the control involved spontaneous abortion in some animals. When rats were placed in the centrifuge starting on day 14 of pregnancy, no cases of abortion were observed, but the fetuses were somewhat behind the controls in body weight and size of ossification sites in the skeleton. In the latter case, the pattern observed with hypergravity of 2 g was virtually analogous to changes occurring in the mother-fetus system in response to exposure during this period to weightlessness on COSMOS-1514.

The commonality of response of the mother-fetus system to weightlessness and hypergravity during late stages of development suggests that there might be a similar commonality during the early stages as well. Based on results of the 2-g centrifugation experiments, it should be possible to impregnate females and realize a complete cycle of prenatal development in mammals under space flight conditions. For such an experiment, it would be best to use intact animals, bred under space flight conditions after completion of the acute period of adaptation to weightlessness.

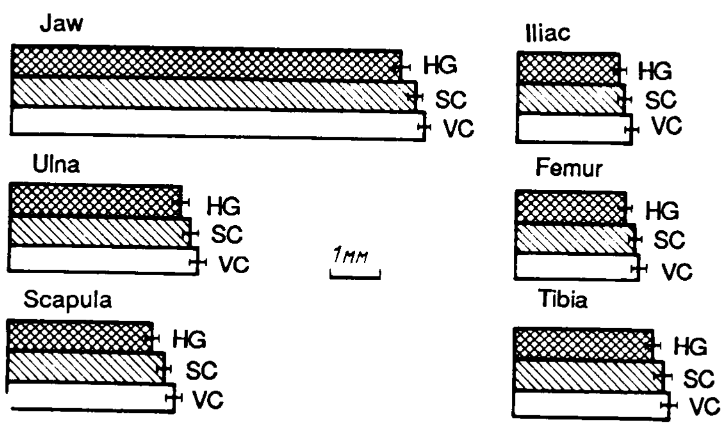


Figure 49: Length of bone sections in 21-day old fetuses developing under conditions of hypergravity (HG) from day 7 to 21 of the prenatal period

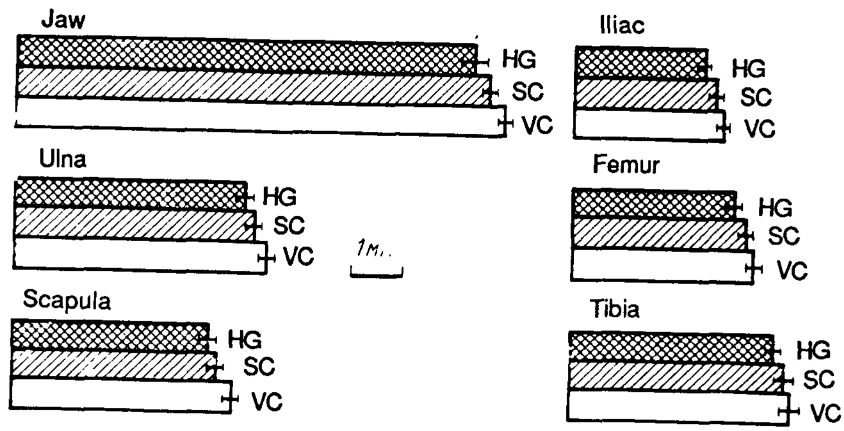


Figure 50: Length of bone ?? in neonate rats developing under conditions of hypergravity from day 7 of the prenatal period until birth

HABITABILITY AND ENVIRONMENTAL EFFECTS

PAPERS:

P988(22/89)* Nefedov YuG, Adamovich BA.
Habitability and life support.
Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.
22(6): 23-29; 1988.
(No references)

Habitability and Environmental Effects, Environmental Factors, Atmospheric Contaminants, Outgassing; Microbiology, Automicroflora, Disinfection; Personal Hygiene, Dust, Noise, Air Regeneration and Conditioning, Water Reclamation; Nutrition, Cosmonaut Rations, Waste Disposal
Humans, Animals, Review Article
Space Station, Mir, Life Support Systems, Pressurized Living Quarters

Abstract: The authors list the factors inherent in space station living conditions and likely to affect humans and animals as: absence or decrease in gravity, background galactic radiation appreciably above that of Earth, absence of ultraviolet radiation, altered parameters of the ambient magnetic field, and sanitary and hygienic factors associated with long-term inhabitation of a pressurized environment. Due to these factors, the relationship between man and his environment is necessarily different in space than on Earth. On Earth vital processes depend on environmental influences, while in a small, pressurized living space vital activity also alters environmental factors.

One of the most important habitability factors revealed by ground-based studies of small sealed environments is altered chemical composition of the air. Studies have shown that expired gas is one of the primary sources of air pollution in such quarters. Major contaminants identified in human expired gas in sealed living spaces include: acetaldehyde, formaldehyde, acetone, methylethylketone, propionic aldehyde, ethanol, methanol, propanol, isopropanol, formic, acetic, propionic, isovaleric, and valeric acids, ammonia, dimethylamine, methane, ethane, ethylene, propane, hexane, and carbon monoxide. Soviet scientists set maximum acceptable levels of virtually all these components as a function of space flight duration. In addition to human generated air pollution, outgassing of polymers used in cabin construction are considered a major problem. A total of 200 synthetic materials have been identified in products of polymer outgassing, including highly toxic substances such as carbon monoxide, epichlorohydrin, hydrocyanide, flouride, acrylonitrile, etc.

During long-term space flight conditions exist for alteration of environmental and cosmonaut automicroflora. At the same time long-term exposure to space may weaken human resistance to microflora. Evidence of changes both of microbiological populations and human immune factors have been demonstrated both in ground-based isolation experiments and in space flight; Quantitative and qualitative changes in microflora have been confirmed. Of particular concern are results such as those showing that staphylococcus increase in toxicity after long-term habitation of closed environments. Inner surfaces of spacecraft cabins have been found to be highly conducive to multiplication of microorganisms, including opportunistic pathogens. The Soviets have actively sought methods to reduce microbial pollution of the interior surfaces of pressurized cabins; however, the germicidal agents had to meet standards for safety during long-term habitation of sealed cabins. While the most effective cleaning product was a 3-6% solution of hydrogen peroxide, this was found to irritate the eyes and mucous membranes. A 1% solution was also found to be effective, without the negative side effects.

Personal hygiene products used in space must occupy as little room as possible and use minimum amounts of water and power. In addition, to cleaning the body in a physical - chemical

sense, they also should aid in maintaining microflora of the skin and hair within healthful limits. Special clothing and bedclothes were developed for this purpose, and bactericidal substances and those intended to reinforce the barrier function of the skin and mucous membranes were included for personal hygiene.

On Mir, data is continuously collected for sanitary-hygienic research including the following components:

- investigation of the distribution of microcontaminants in the atmosphere of the major inhabited areas of the station;

- investigation of the quantitative and species composition of the microflora of crewmembers and the environment;

- sanitary chemical research on the atmosphere of the inhabited compartments;

- study of the thermal conditions of the living environment and the rate of airflow;

- investigation of the major characteristics of background noise and dust conditions.

These results were used as the basis for developing sanitary and hygienic measures.

Life support system reserach and development in the Soviet Union is based on Vernadskiy's concept of the evolution of the biosphere and arose from the theories and technology of aviation medicine and study of underwater environments. It is considered that to support normal human existence during space flight, 800 g oxygen, 2500 g potable water, and about 700 g (3000-3500 calories) must be provided per cosmonaut per day.

Air regeneration and conditioning in some sections of Mir depend on supplies of chemically bound oxygen in the form of superoxides of alkaline materials. Water vapor is absorbed by the sorbents producing oxygen, while alkalis absorb carbon dioxide, forming carbonate and water and then bicarbonate. Other components of the station utilize more advanced processes (not described). Oxygen and carbon dioxide proportions in the air are controlled automatically using a gas analyzer. Separate regenerative filters are used to get rid of unpleasant odors and other contaminants.

Essential supplies of potable water are stored in special containers and preserved by silver ions. Special water-disinfecting cartridges have also been developed for emergencies or ultra long-term situations. However, neither of these methods will be the primary one for future long-term flights. A system reclaiming water from human waste water is already being developed. Virtually all Salyut and Mir crews have used a system which reclaims atmospheric moisture and produces potable water. In this system water condenses on the surface of refrigeration-desiccation units, then accumulates in an accumulator. Organic and inorganic condensates are removed from the water as it is passed through cartridges with specially developed ion-exchange resins and activated charcoal and through a special device for enrichment with essential minerals. The system also contains a unit for heating the water for use with freeze-dried food and in the washing facility.

Cosmonaut rations are divided into four daily meals and consist mainly of sterilized products and dishes packed in cans and aluminum tubes. The mean daily ration weighs approximately 1400 g and supplies 3300 calories. There is a special device with a timer and bell to heat food. Rations are supplemented based on cosmonaut tastes. Freeze-dried foods are also provided, and will be the main source of food on flights where water reclamation will occur on a fuller scale. Freeze-dried products are desirable due to their low weight, retention of nutritive and aesthetic qualities, and the fact that fermentation is slowed and growth of microbes curtailed. Devices for rehydrating food in space have already been developed.

Housekeeping and sanitary measures on Mir include creation of a space shower, a lavatory, marking of "top" and "bottom" of the interior with paint, and development of a dinner table with containers for the daily rations of six cosmonaut and a special chute for wastes.

An air-cleaning system removes harmful organic and inorganic substances from the air. Wastes are packed in special containers and disposed of after accumulating in sufficient quantities.

With the goal of eventually creating closed biological life support systems for space crews, considerable work has already been done on space greenhouses One such system was tested for a year with three subjects; this was the first test of a number of systems subsequently used on Salyut and Mir.

HEMATOLOGY

PAPER:

P1025(22/89)* Zukhbaya TM, Smirnova OA.
On the stimulating effect of prolonged low-dose-rate exposure to radiation on mammalian lymphopoiesis.
Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.
23(1): 47-51; 1989.
(11 references; 2 in English)

Hematology, Lymphopoiesis, Bone Marrow
Rats, Female
Radiobiology, γ-Radiation, Low Doses, Long-Term, Mathematical Modeling

Abstract: Subjects in this experiment were white outbred female rats exposed for 22 hours per day to a field of γ-radiation from ^{137}Cs with dose-rates of 0.1, 0.4, 0.8, 1.1, 2.0 ,and 4.0 Gy/day. Measurements were made at different times during exposure and included absolute number of lymphocytes in peripheral blood. Absolute level of lymphocytes in bone marrow of the femur was measured using a myelogram from smears of bone marrow of one femur, and the total number of bone marrow cells was computed for the other femur. F and t statistics were computed and used to determine statistical significance. Non-irradiated animals of the same age were used as controls. Data obtained were compared to data generated by a mathematical model of lymphopoiesis, similar to the one described in Abstract P1023 (Mathematical Modeling). The three types of cells modeled were bone marrow precursor cells, from stem cells to morphologically identifiable, dividing lymphoblasts; non-dividing maturing lymphocytes; and mature blood lymphocytes. The cells were divided into three groups on the basis of their response to radiation. The first group included unharmed cells or those capable of reparation, the second group included damaged cells dying after 1 to 2 days, and the third group included cells dying 4-6 hours after irradiation. Variables were the concentrations of the three types of cells as well as the specific inhibitor of mitosis, chalone (I). Parameters were introduced to represent death rate due to radiation and rate at which unharmed cells become damaged and severely damaged cells. An additional parameter was the rate of emission of chalone by living and dead cells of the different types. Values were generated for the model using a computer.

The model predicts that at some dose rate interval, the new stationary concentrations of lymphoid elements in bone marrow of irradiated animals is higher than in nonirradiated counterparts. This prediction is confirmed by experimental observations. The model also predicts that prolonged low-dose rate irradiation will stimulate reparative processes in the lymphopoietic system. This prediction is also confirmed. The authors argue that their data suggests that special *ad hoc* hypotheses need not be introduced to account for the stimulating effect of exposure to low-dose radiation on lymphopoiesis. Instead, this effect may be explained within the framework of the chalone theory of hemopoietic regulation. The observed effect is caused by elevated levels of lymphoid elements in bone marrow and increases in their mitotic activity in mammals exposed to long periods of low-dose-rate radiation.

Table: Parameters of the lymphopoiesis model

Figure 1: New stationary values of dimensionless concentrations of cells of different types as a function of dose rate of chronic irradiation

Figure 2: Changes over time in lymphopoiesis in rats undergoing chronic irradiations with dose rate of N=0,1 Gy/day.

Figure 3: Changes over time in lymphopoiesis after acute irradiation in a dose of D=1 Gy, in rats not previously exposed to radiation and those exposed for a long period to dose rate of N=0.1 Gy/day.

HUMAN PERFORMANCE

PAPERS:

P995(22/89) Yevstaf'yev VN, Netudykhatka OYu.
The effects of physical exercise and optimization of work rest schedules on the work capacity of sailors on long-term cruises
Teoriya i praktika fizicheskoy kul'tury.
1988(7): 4-6.
[8 references; none in English]

Human Performance, Work Capacity
Humans, Males, Sailors
Physical Exercise, Work-Rest Schedules

Abstract: A total of 250 males, aged 19-40, who had worked as sailors no less than 1 year and had been pronounced fit for work were studied during long-term cruises. Physical work capacity was measured by a step test and with a bicycle ergometer. PWC_{170}, VO_{2max}, and a step test index were computed. Maximum muscle strength in the hands and tolerance of static loading were also measured using a manual dynamometer. Physical work capacity first increased (up to days 30-45), then stabilized for up to 60-120, days and then decreased. In sailors on ships with good working conditions the period of decrease occurred at approximately 105-120 days. As the cruise continued, this level continued to drop, reaching a minimum (132 W) on days 170-180. Sailors working on tankers, and ships carrying gas and chemicals, who were exposed to higher levels of stress, exertion, and toxic factors, showed a decrease in work capacity starting at approximately day 70. Their work capacity was approximately 11% lower than sailors on other types of ships at the start of the cruise, and 26% below at the end of the cruise. Muscle strength followed a similar pattern of increase, stabilization, decrease.

When sailors on long cruises participated in physical workout programs for 10-15 minutes a day and were given access to a gymnasium with rowing machines and bicycle ergometers, physical work capacity increased by 18% compared to levels before the cruise and 22% compared to levels after the cruise; muscle strength did not decline.

P999(22/89) Pogoreleov IA, Shimanovich YeG.
The physiological mechanisms of autogenic training and its use with sailors on long-term cruises.
Voyenno-Meditsinskiy Zhurnal.
1988(7):57-58.
[7 references; none in English]
Authors' affiliation: Medical Corps

Human Performance
Humans, Sailors
Long-Term Cruises, Autogenic Training

Abstract: The authors used the methods of autogenic training [a combination of suggestion and autosuggestion directed at relaxation; See Digest Issue 9], with sailors of the fishing fleet on long term cruises. Sailors underwent one session a day before going to bed in their cabins. Sessions were controlled by a tape recording in which the verbal content [relaxation suggestions] was accompanied by soothing music. Sailors had previously been instructed in the techniques by medical personnel. Subjects in the study were 52 sailors, aged 20 to 28. All of them were undergoing a series of other treatments, (physical exercise, vitamin supplements, ultraviolet irradiation, etc.). Of the total, 30 sailors were exposed to autogenic training and 22 served as controls. On day 45 of each cruise, subjects filled out a questionnaire listing 30 complaints of an asthenic/neurotic nature. Then they underwent a course (10 sessions daily; sic., unclear how this related to the bedtime session) of autogenic training. On day 60, all subjects responded to the same questionnaire.

Responses were scored using a 3-point rating scale (1 = general condition unchanged; 2 = general condition significantly improved; 3 = stable improvement in general condition, no neurotic symptoms). In the experimental group, 3 subjects (10%) were scored as "1"; 16 subjects (52.8%) as "2"; and 11 (37.2%) as "3." The general condition of the control group was virtually unchanged.

LIFE SUPPORT SYSTEMS

PAPERS:

P989(22/89) Meleshko GI, Shepelev YeYa.
Man-rated biological life support systems .
Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.
22(6): 30-36; 1988.
(No references.)

Life Support Systems, CELSS, Man-Algae-Waste Mineralization System; Man-Algae-Higher Plants, Botany
Theoretical Article
Space Flight, Biospherics

Abstract: Soviet attempts to devise man-rated biological life support systems for use in space have been based on the principle that such systems must be functional analogs to biocenoses on Earth, i.e., these systems must reproduce in principle the major properties and mechanisms of natural substance cycles, if they are to create a living environment adequate to human requirements. In particular, such artificial systems must reproduce the hierarchical functional and structural organization of natural ecosystems, with lower levels of organization subordinate to higher ones, maximal retention and utilization of natural associations among organisms to form the basis for internal self-regulation mechanisms, and ecological stability. This concept is contrasted in the paper with the "biotechnological" concept, in accordance with which the creation of a closed ecological substance cycle is based on development of highly productive technology and devices for cultivating organisms. while uniting them into an integrated functional system is a matter of technology and automated control.

The system development strategy employed by the Soviets has involved: 1) study of different species and the optimal conditions for growing them in highly dense populations; development of the technology to support continuous cultivation] (of plants and algae) on the basis of a new type of mineral nourishment; 3) and study of the functional characteristics of highly productive populations and communities of organisms and their stability over time. On the basis of the results obtained, they worked out material balances and developed functional system components. Other issues were the effects of the subjects selected on the atmosphere, their concomitant microflora, and possible ways to use the wastes that accumulate within the system. Soviet scientists developed and studied a number of model systems for supporting human life, varying in biocenotic structures, sizes, and functional parameters, all based on algae, higher plants and microorganisms.

One such system, 5 m^3 in area, involved 30 liters of suspended algae with a density of 10-12 g dry substance in 1 l, and 59 l water containing the algae. The system was studied in operation 5 times for 30-31 days. In addition to humans, the model contained a component for biological mineralization of urine and a device for drying the algal biomass, human solid wastes and evaporation of urine to return the moisture it contained to the material cycle. System closure was incomplete due to mineral salts added for nourishing the algae and freeze-dried food for the humans, to which was added 50 g of dry substance from the algae. Everything else needed for human life support was produced by the system. All water used was produced by the system and processed in a photosynthetic reactor; some condensate was set aside for drinking water for which if was cleaned through sorption. Oxygen balance in the atmosphere was achieved through regulation of the productivity of the photosynthetic reactor. Approximately 5% of the CO_2 produced by the humans was not used by the algae and had to be removed. Soluble gaseous contaminants produced by the system were absorbed by the algae and only detected in trace quantities in the atmosphere. Relatively insoluble contaminants (carbon monoxide and methane) accumulated in the atmosphere and then stabilized. Carbon monoxide levels reached an

average of 20 mg/m^3 and methane 150-150 mg/m^3. During the month-long period the system operated, aside from disruption of the CO_2 balance, no signs of nonstationarity were detected. Over the period the initial level of algae was regenerated 15 times. The stability of the system was based on the stability of the characteristics of the algae culture. When a portion of the cells were destroyed through an accident, their numbers were restored.

Study of the major characteristics of the environment created by the system showed that, aside from regenerating air and water, the algae removed water-soluble volatile contaminants from the atmosphere, stabilized the total number and species distribution of human indigenous bacteria, maintained atmospheric ions at an optimal level, and limited the number of aerosol particles and dust in the atmosphere. In summary, the model system completely regenerated the atmosphere, utilized 95% of the carbon dioxide, and produced up to 10% of the food.

More complex systems utilizing higher plants (man-algae-higher plants-mineralization) were studied in 23 experiments lasting 1.5 to 2 months. The growing area for the plants was 15 m^2, of which 11.25 m^2 was devoted to wheat and the remainder to various vegetables (peas, beets, carrots, cabbage). Inclusion of a photoautotrophic component and higher plants optimized parameters and increased closure. Oxygen and CO_2 balance were completely maintained. Food regeneration increased to 26%. Increased closure of trophic bonds could be achieved by optimizing plant growing technology and utilizing portions of the plants not traditionally used as food. Overall regeneration increased from the previous system by only 2% (90 to 92%). However, plants not only increased closure but provided nutrients essential to humans. The authors state that, because plants must exceed the mass of the heterotrophic organisms by a large amount in order to support a closed system, a system to be used in spacecraft, where area is limited will probably use a combination of higher plants and one-celled algae for the photoautotrophic component.

Inclusion of animals in the system will improve closure only slightly, although their presence is dictated by the need to meet human nutritional needs. Because the animal component has such a high "cost" in terms of energy use, the minimal necessary biomass is likely to be included in a life support system. The Soviets have not yet studied animals within a system model, although a functional component based on animals has been developed using traditional animal food (birds) as well as nontraditional (soft-shelled mollusks). Analysis showed that during initial attempts to integrate this component into the system, rather than have humans consume the biomass of the animals, it would be better to have them eat the eggs. This consideration has led to tentative plans to use the quail as the first variant of the heterotrophic component in future models, although these birds to some extent compete with man for food. Animals that would not compete for food by consuming plant and even human waste tend not to be traditional food sources.

The following paragraphs summarize the tentative general conclusions that can be drawn from 30 years of work in the Institute of Biomedical Problems on biological life support systems:.

1. It has been demonstrated both theoretically and experimentally that it is possible to create the simplest human biological life support system based on the photosynthesis of one-celled algae. This system can serve independently to regenerate the atmosphere, water, and some food, and may be implemented on spacecraft prior to the development of more complex systems utilizing plants and animals.

2. The results that have been obtained provide a basis for transition to the next stage of research -- the creation and study of system models with a more complex biogeocentric structure and a greater degree of closure. The models that have been studied have made it possible to progress to experimental study of the most general principles for creating biological life support systems that cannot be deduced directly from general ecology. The

most important of these are possible minimal parameters of the system (size, weight, species structure), the ratio of living and inert substances, the ratio between producers and consumers, and others.

Table 1: Extent of regeneration of substances in man-algae-mineralization and man-algae-higher plants-mineralization systems

Substance	Consump. g/day	System: man-algae-mineralization, Regeneration g/day	%	man-algae-higher-plant-mineralization, Regeneration g/day	%
Oxygen	755	755	100	755	100
Food	530	50	9	138	26
Water	3400	3400	100	3400	100
Total	4685	4205	90	4293	92

Table 2: Ratio (in g/g dry substance) of components of the environment to biomass in systems of various sizes

Environmenta component	Biosphere as a whole	Subtropical rain forest with "own" atmosphere	Systems: man-algae-plants 50 m^3 per man	man-algae-mineralization, 5 m^3 per man
Atmosphere	$2.1 \cdot 10^3$	88	2.5	$3.2 \cdot 10^{-1}$
Oxygen	$4.9 \cdot 10^2$	19.7	0.5	$7.1 \cdot 10^{-2}$
Carbon dioxide	1.02	$4.0 \cdot 10^{-2}$	$5 \cdot 10^{-2}$	$5 \cdot 10^{-2}$
Water	$5.7 \cdot 10^5$	- -	26	3.0

P1029(22/89)* Pak Z, Sytnikkova, NN, Berlin AA, Koloskova YuS, Shirobokov VP, Tyshko AG.
Hygienic aspects of wash water reclamation systems.
Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.
23(1): 67-70; 1989.
[5 references; none in English]

Personal Hygiene, Wash Water
Humans, Males and Females, Individual Differences
Life Support System, Water Regeneration System, System Test, Detergents

Abstract: This paper describes a test of a wash water regeneration system. The functioning of the system and the hygienic evaluation of the quality of the reclaimed water were examined in the context of a test in which male and female subjects were allowed only a single shower per week using 10 liters of water obtained from the reclamation system. Used wash water was collected after the shower and the following physical chemical parameters were measured: bichromate oxidizability, electrical conductance, hardness, odor, transparency, concentration of detergent, chloride ions, and ammonium nitrite. Water parameters were studied after showers with or without detergents. In addition, the number of viable microorganisms were counted in 1 ml. Pure cultures were obtained from sample colonies of wash water for subsequent identification of morphological, cultural, and biochemical parameters.

It was found that the parameters producing the most information in comparative evaluation of individual differences in wash water used by different subjects were pH, chemical oxygen parameter, electrical conductivity and concentration of chlorides. Individual differences were relatively pronounced, which the authors attribute to innate differences in skin oiliness. Wash water containing higher concentrations of organic contaminants was also higher in chlorides. Total concentration of microorganisms in wash water without use of detergents fluctuated between 1.104 and 1.105 microbial bodies per ml. Microbial parameters for women were close to those for men. The most numerous microorganism was staphylococcus. Other organisms found represented the natural microflora of human skin. These studies confirmed the desirability of using detergents with disinfecting properties. When detergents were used for showers, total number of microorganisms decreased to $8 \cdot 10^2$ - $6 \cdot 10^3$ bodies per ml. When detergents were allowed to remain on the body for 3 - 5 minutes, the wash water contained very few microorganisms Use of detergents also increased the concentrations of organic substances and chlorides in used wash water. Organic contaminants in the water included not only surface dirt on the skin, but products of secretion of sebaceous and sweat glands. This suggests that serious consideration should be given to the effects of the specific detergent used on the functional status of human skin.

Table 1: Physical/chemical composition of used wash water without use of detergents

Table 2: Physical/chemical composition of used wash water with the use of detergent

Figure 1: Oxidizability of used wash water obtained from various subjects

Figure 2: Concentration of chlorides in used wash water obtained from various subjects

P1030(22/89)* Lebedeva TYe, Nazarov NM, Chizhov SV.

Study of the effectiveness of urine preservatives within water reclamation systems.

Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.
23(1): 70-74; 1989.
[7 references; 1 in English]

Urine Preservation, Microbiology, Bacteria
Humans
Life Support Systems; Water Reclamation Systems

Abstract: On long-term space flights it is desirable to use urine within the water reclamation system; however, the urine must be preserved before it enters the reclamation system to kill microorganisms and prevent hydrolysis of urea, which pollutes the atmosphere with ammonia. In preliminary studies, a number of existing Soviet disinfectants were studied. However, the antimicrobial properties of these substances decreased in the presence of certain components of urine. Thus new disinfectants had to be found. A total of 11 such substances were tested in the study described here. They included: complex organic chlorine containing substances R_1-Cl (1) and R_2-Cl (2); iodine containing substances - iodine and potassium iodide (3, 4); a chromium containing complex preservative (5); organic and mineral acids R_3(6), R_4(7); nitrolactic acid (8); carbolic acid (9); urotropine (10); and boric acid (11). Test cultures of microorganisms used included thermostable strains of *Bacillus antracoides,* intestinal bacilli, *Staphylococcus aureus,* and representatives of microflora of airtight living spaces which actively hydrolyze urea, *Proteus mirabilis, Pseudomonas aeruginosa* and typical urobacteria: *Sporosarcina urae, Micrococcus varians,* and *Micrococcus luteus.* Cultures of microorganisms (or spores) 24 hours old were placed in sterile urine in a concentration of 106 kl/ml, which contained varying concentrations of preservative. Experiments were repeated 6-9 times at room temperature. The bactericide and sporocide effects were evaluated from the absence of subsequent growth of the bacteria on solid agarized mediums: meat peptone agar (MPA), MPA with urea, or Endo medium 1, 4, and 24 hours after contact with the preservative. Cultures were further checked for absence of colony growth 1 and 7 days after neutralization of the preservative. Results were subjected to statistical analysis.

The most effective agents were the chlorine containing substances (1 and 2), which after exposure of 1 hour had a sporocidal effect in concentrations of 2 and 4 g/l, respectively. *Escherichia coli, Staphylococcus aureus, Pseudomonas aeruginosa,* and *Proteus mirabilis* died after 1 hour at concentrations of 1-2 g/l. Concentrations of these preservatives of 0.5 g/l had a bactericidal effect after 1 day. Preservatives containing iodine were only slightly less effective than those containing chlorine. The only other preparation with a sporocidal effect was number 6 (described as an organic and mineral acid). Preparations 4 and 5 were also relatively effective against bacteria. The least effective substances were urotropine and boric acid. The first five substances were tested further. The antimicrobial properties of the first two chlorine-containing preservatives were tested in water, where they required only one-quarter to one-half the dose to act as bactericides and sporocides. These substances also had a lasting effect, retaining their antimicrobial properties even after a year of storage in urine, although their antimicrobial activity decreased by a factor of 2-4. When substance 1 was added to the complex chromium-containing preservative 5 and used to reclaim water from urine using the method of low-temperature vaporization from the surface of porous elements, the water obtained after sorption cleaning and adjustment of mineral components met Soviet standards for drinking water Haloid-containing agents are recommended for use to preserve urine in water reclamation systems for space flights.

Table 1: Bactericidal (sporocidal) concentrations of preservatives in urine

Table 2: Bactericidal (sporocidal) concentrations of preservatives in water

Figure: Bactericidal activity of agent 1 over time

P1032(22/89)*Vasilenko II, Fedosova AN, Shevel' NM, Sinyak YuYe.

Use of hydrogen peroxide and iron-containing catalysts to remove phenol from water.

Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.
23(1): 76-79; 1989.
[20 references; 6 in English]

Life Support Systems, Water Reclamation, Urine Recycling
Chemical Experiment
Phenol, Hydrogen Peroxide, Iron-Containing Catalysts

Abstract: Phenol is one of the toxic components of urine that would have to be removed for urine to be used in a water reclamation system. This work studied the heterogeneous liquid phase oxidation of phenol by hydrogen peroxide on minerals containing iron in their oxides, hydrooxide, magnetite, and siderite. These minerals were selected because of their availability and nontoxicity and their high capacity for oxidation. Preparation of the catalysts consisted of pulverizing the sample. Concentrations of iron, and its oxidized and reduced forms, were measured. The catalysts were immersed in a water solution of phenol with a concentration of from 0.025 to 01 M analytic grade C_6H_5OH. Hydrogen peroxide in the form of a 9.6M solution of chemically pure H_2O mixer was added and mixed with a magnetic stirrer. Rate of emission of oxygen and carbon dioxide was monitored gasometrically, and the hydrogen parameter of the solutions was measured with a potentiometer.

The compounds Fe_2O_3 and $Fe_2O_3 \cdot 2Fe(OH)_3$ did not act as catalysts for the destructive oxidation of phenol by hydrogen peroxide. Minerals containing 8.7% Fe^{2+} as part of magnetite Fe_3O_4 did act as catalysts, but at normal temperatures the process was very slow and conversion of the phenol was low. Siderite was found to be an active heterogeneous catalyst for the destructive oxidation of phenol by hydrogen peroxide in its liquid phase. The output of carbon dioxide and the utilization factor for the oxidant are determined by the ratio of components and the kinetics of the partial catalytic reactions. A high degree of conversion of phenol into carbon dioxide can be achieved without heating or increasing pressure above normal values, which makes this compound promising for use in water purification and reclamation in life support systems with limited energy supplies.

Table: Conversion of phenol with multiple uses of the catalyst

Figure 1: Kinetics of emission of carbon dioxide at various concentration of phenol

Figure 2: Effects of concentration of the catalyst on rate of phenol oxidation

Figure 3: Volume of carbon dioxide and oxygen at various pH of solutions of phenol and 0.5 g catalysts

P1038(22/89)* Chernyakov IN.
Effectiveness of oxygen equipment within a life support system for stratospheric flight.
Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.
23(1): 11-16; 1989.
[52 references; 18 in English]

Life Support Systems, Oxygen Equipment
Equipment and Instrumentation, Systems Test
Aircraft Flight, Stratospheric

Abstract: This paper describes oxygen equipment for use on stratospheric flights, discusses the major factors limiting or determining the effects of such systems, and identifies ways in which this equipment will be improved in the future. The major types of equipment are: 1) a system consisting of an oxygen mask, protective helmet, and oxygen unit; 2) the same system with a partial pressure suit; 3) a set including a partial pressure suit, with partial pressure boots and gloves and a pressurized helmet. The first type of system has a maximum tolerable value of excess pressure of 25-30 mm Hg and is usable at a maximum altitude of 15 km, with an absolute intrapulmonary pressure at that altitude of 115-1120 mm Hg. The time to unconsciousness at maximum altitude is 5-10 minutes. In such systems the development of acute hypoxic hypoxia, due to low levels of alveolar pressure and circulatory hypoxia resulting from pooling of blood from the periphery and decreased venous return with excess pulmonary pressure, limits the tolerable exposure to 15 km for such systems. Such systems are used only for short-term life support during emergencies.

The inclusion of a partial pressure suit creating external counterpressure on the limbs and body has made it possible to increase the maximum tolerable pressure to 75 mm Hg, and the maximum altitude to 18 km, with absolute pressure in the lungs at this height of 130 mm Hg. Addition of the suit decreases the extent of hypoxic hypoxia. However, at 18 km, time to unconsciousness is still only 5-10 minutes due to circulatory hypoxia and the difficulty in breathing with excess pressure of 75 mm Hg. Tolerance time at 18 km in such a system is limited by problems in portions of the body not protected by the suit (neck, eyes, ears, mouth). Problems include pain in the mouth and difficulty in articulation, burst blood vessels in the eyes, excess pressure on the ear drum, and decreased acuity of vision and hearing. Replacement of the oxygen mask by a pressurized helmet and addition of partial pressure foot and hand coverings makes it possible to increase excess intrapulmonary pressure to 145-150 mm Hg and solve the problem of the "altitude barrier." With the level of excess pressure provided by such systems, satisfactory oxygen conditions can be maintained even at very high altitudes. However, actual time during which work capacity is maintained with such systems at 25 km is only about 10 minutes. Thus, these systems can only be used as means to save the pilot on stratospheric flight when the cabin loses pressure. The shortcomings of these systems are associated with design problems. For example, the tension device in the suit creates inhomogeneous counterpressure to the excess pressure in the lungs, so that some portions are over- and some underpressurized, which can lead to pain and disruption of circulation. Another problem is the stiffness and rigidity of the chambers when excess pressure increases in the suit. This impedes the rise and fall of the chest and interferes with movement, leading rapidly to fatigue. The helmet makes head movement difficult and restricts vision. When depressurization is explosive, the suit cannot compensate rapidly enough for the increased intrapulmonary pressure,and pilot work capacity may be severely impaired.

The author notes two directions for further improvement of such systems. The first involves development of systems that are more comfortable to wear under routine conditions in a pressurized cabin. One possibility for providing freer movement would be a suit without sleeves. Antigravity suits could also be used. Such systems would not permit a very high

altitude flight to continue even after cabin depressurization, but could allow the pilot to drop down safely to 12 km and continue the flight. The second direction of improvement involves development of oxygen systems that would allow pilots and crew to perform all their tasks in a depressurized cabin at very high altitudes. This would require improvements in the efficiency of the oxygen systems. One recommendation would be to allow the excess pressure to vary as a function of phase of breathing cycle, so as to facilitate cardiovascular functioning and respiration. Also recommended is use of pneumomechanic tension creating devices in the suits with a single pressure in the breathing and pressure line. Use of elastic materials that extend in only one direction for the suit shell would decrease rigidity and thus discomfort.

MATHEMATICAL MODELING

PAPER:

P1023(22/89)* Smirnova OA
Mathematical modeling of the cyclic kinetics of hemopiesis.
Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.
23(1): 41-45; 1989.
[12 references; 5 in English]

Mathematical Modeling
Mammals
Hematology, Hemopoiesis

Abstract: Mathematical models were constructed of the formation of lymphocytes, thrombocytes, and granulocytes in mammals. The models were realized as systems of nonlinear differential equations, with variables representing concentrations of mature blood cells and their precursors in bone marrow. The models included representation of chalone inhibition of rate of propagation of bone marrow blast cells, and reflected the major stages in the development of hemopoietic cells, and the individual characteristics of the different types of cells: the presence of a bone marrow "depot" of granulocytes, instability of the mean lifetime of erythrocytes, and the mean number of genomes contained by megakaryocytoblasts. Testing using the qualitative theory of differential equations, oscillation theory, and computer generated values demonstrated that the model reproduced all empirically observed dynamic characteristics of the hemopoietic system. Depending on the values of the kinetic parameters, the recovery process of all types of hemopoiesis may either be aperiodic or take the form of damped or stable oscillations. The conditions under which stable oscillations arise (limit cycles) are discussed. Using the model, a computer generated values for the period and amplitude of stable concentrations of cells that agreed in each case with empirical data. The authors conclude that the models can be used to simulate biological rhythms with a period of about a month in the hemopoietic system; they thus can be useful in analysis of flight data and the hemopoietic effects of space flight factors.

The model of the formation of each type of cell considered: bone marrow precursor cells from the stage of stem cell to the stage of morphologically identifiable mitosis (X), nondividing maturing bone marrow cells (Y), and mature blood cells (Z). Changes in concentrations of these three types of cells (x., y,. and z, respectively) and concentrations of the specific chalone I were described by a system of differential equations.

$$\begin{aligned} dx/dt &= B(I)\,x - Cx, \\ dy/dt &= Cx - Fy, \\ dz/dt &= Fy - Ez, \\ dI/dt &= G(x + \theta_1 y + \theta_2 z) - H \cdot I. \end{aligned}$$

C and F refer to the rate of passage from groups X into Y, and Y into Z; E is the rate of natural death of Z cells. G, $G\Theta_1$, $G\Theta_2$ are the rates of increase in concentration of the inhibitor, resulting from vital activity and the death of X, Y, and Z cells, and H is the rate of chalone disintegration. B(I) is the rate of multiplication of X cells which can be represented by the formula.

$$B(I) = \alpha/(1 + I/K_i),$$

where α is the maximum rate of mitosis of X cells and Ki is the inhibitor constant.

C, F and E could either be a constant or a nonlinear function of the concentration of the appropriate cells.

Figure 1: Stable oscillations of concentrations of lymphocytes (a), thrombocytes (b), and erythrocytes (c)

Figure 2: Cyclic kinetics of granulocytopoiesis

METABOLISM

PAPERS:

P997(22/89) Meyerson FZ, Arkhipenko YuV, Didenko VV.
Selective suppression of lipid peroxidation in the brain in response to stress.
Byulleten' Eksperimental'noy Biologii i Meditsiny.
1988(11):542-544.
[7 references; 2 in English]
Authors' affiliation: Institute of General Pathology and Pathological Physiology, USSR Academy of Medicine, Moscow

Metabolism, Lipid Peroxidation; Neurophysiology, Brain
Rats, Males
Psychology, Stress

Abstract: This study tested the hypothesis that the brain is selectively protected during stress by comparing the effects of stress on lipid peroxidation (LP) in the brain, liver, and heart. Subjects were male Wistar rats (n not specified) divided into four groups. Group 1 was a control and groups 2, 3, and 4, were exposed to 2, 3, and 4 hours of immobilization stress, respectively. Immobilization was achieved through rigid restraint in a supine position. The animals were sacrificed 2 hours after treatment termination. LP in the brain, heart and liver was assessed by determining *in vivo* concentration of the intermediate peroxidation product malonic dialdehyde, and by investigating the induction of LP in tissue homogenates *in vitro* . To perform the latter tests, the organs were isolated, washed, and stored in liquid nitrogen. Tissue was homgenized in cold in a medium containing 50 mM, tris-HCL, 100 mM NaCl (pH 7.4) with the weight of the tissue and volume of solution in a ratio of 1:4. After filtration, concentration of protein was measured using the biuret reaction. LP was induced *in vitro* with a system of ascorbate, + Fe^{2+} (50 μM+ 5 μM). After measurment of initial level of LP products, the reaction was triggered by adding a solution of ascorbate + Fe^{2+}. LP products were measured spectrophotometrically using 2-thiobarbituric acid. Data were processed statistically using t tests and correlation coefficients.

In the controls, concentration of malonic dehydrogenase was approximately the same in the three tissues studied. One hour of immobilization stress increased malonic dialdehyde in the heart and liver, but with decreased (by a factor of two) concentrations in the brain. When Fe^{2+} and ascorbate were added to tissue, lipid peroxidation increased by a factor of 3 in the heart and liver (compared to control) and decreased by a factor of 2.3 in the brain. After 6 hours of stress, concentration of malonic dialdehyde was only slightly above the norm in the tissue of the heart and liver and remained depressed in the brain. After 12 hours of immobilization, malonic dialdehyde concentrations had dropped to normal levels in the heart and liver, and were slightly elevated in the brain. Individual rats with the highest concentration of products of lipid peroxidation in the heart and liver (presumably after 1 hour of stress) had the lowest concentrations in the brain.

The author concludes that the rapid suppression of lipid peroxidation and protection of the membrane structures of the brain may be highly significant in acute stress situations, where it is critical for the brain to function well. It is important to find out how long this defense mechanism operates and to determine which component of the stress reaction is responsible for suppression of lipid peroxidation in the brain.

Table: Change in the concentration of malonic dialdehyde (in nmole per 1 mg protein) in homogenates of tissues of rats undergoing immobilization stress

Figure: Dynamics of initial rate of formation of malonic dialdehyde in homogenates of rat tissues, prepared after immobilization of different durations

P998(22/89) Meyerson FZ, Tverdokhlib Vp, Nikonorov AA.
Prevention of atherogenic dyslipoproteinemia and metabolic liver disorders in response to emotional pain/stress.
Voprosy Meditsinskoy Khimii,
1988(6):104-109.
[25 references; 8 in English]
Authors' Affiliation, Institute of General Pathology and Pathological Physiology, USSR Academy of Medicine, Moscow; Orenburg Medical Institute

Metabolism, Dyslipoproteinemia, Liver Disorders
Rats, Males
Psychology, Emotional Pain/Stress; Adaptation, Hypoxia; Antioxidants

Abstract: In this experiment male Wistar rats were exposed to the "emotional pain/stress" paradigm (See Abstract 997) for 6 hours. Adaptation to repeated stress was created by exposing the animals to short periods of this treatment, increasing to 60 minutes a day during the 14 days preceding the experiment. Adaptation to hypoxia was effected by exposing the animals to high-altitude conditions in a barochamber, starting at 100 m and gradually increasing to 5000 m in sessions of 6 hours per day for a period of 456 days. The day after the adaptation sessions, animals were exposed to stress for 6 hours. The antioxidant ionol (2,6-Di-tret-butyl-4-methylphenol) was administered orally in a dose of 20 mg per kilogram body weight in 0.5 ml sunflower oil for 3 days before stress induction. The animals were divided into 8 groups: group 1 contained untreated controls; group 2 animals underwent only the emotional pain/stress paradigm and were studied on the subsequent day; group 3 animals were preadapted to short term stress; group 4 rats were preadapted to short-term stress and then exposed to the pain/stress treatment; group 5 animals were adapted to hypoxia; group 6 animals were preadapted to hypoxia and then exposed to the pain/stress treatment; group 7 animals were given ionol; and group 8 animals were given ionol and then exposed to pain stress. In all cases animals were studied the day after pain/stress induction. Blood serum and liver tissue were obtained and processed. Lipid metabolism was assessed in blood by measuring total cholesterol, triglycerides, and cholesterol in high density lipids after precipitation of apo-B-containing lipoproteins, $MnCl_2$ and heparin. An atherogenic index was computed equal to:

$$\frac{\text{Total cholesterol - High Density Cholesterol}}{\text{High Density Cholesterol.}}$$

Information was obtained about lipid peroxidation processes in the liver through measuring malonic dialdehyde (MDA) and activity of superoxide dismutases (SOD) (methods not described). The criterion for liver damage was activity of organ-specific cytoplasmic enzyme — fructose-1-phosphate aldolase (F-1-PA) in blood serum.

High density lipoproteins decreased in response to stress and the atherogenic index increased. These effects reached a maximum (high density lipids halved and atherogenic index quadrupled) 24 hours after stress inducing procedures. Preadapation to gradually increasing hypoxia significantly increased the proportion of high density lipids and decreased triglycerides. The atherogenic index of animals adapted to hypoxia was half that of untreated animals. Exposure of the former to stress produced no significant changes in the cholesterol pattern and led to an even greater decrease of triglycerides in blood serum; atherogenic index did not differ from control. A similar but less pronounced antiatherogenic effect was attributable to adaptation to short periods of stress. When ionol was administered, high density lipids increased and atherogenic index decreased in comparison to the group of unprotected animals. Evidently ionol limits but does not prevent the development of dislipoproteinemia. Under the influence of stress the concentration of MDA doubled in the liver, while the activity of SOD (the major antioxidant enzyme) decreased. SOD activity decreased most sharply 2 hours after stress. Predaptation to

hypoxia or short-term stress not followed by pain/stress led to a reliable increase in SOD activity in the liver, by 66 and 44%, respectively, but affected MDA only slightly. When emotional pain stress occurred after preadaptation, MDA increased by only 17 and 25%. Ionol, like preadaptation, prevented activation of lipid peroxidation and accumulation of MDA after stress, but had no significant effect on SOD activity.

When unprotected animals were exposed to stress, F-1-PA quadrupled in blood serum, reflecting liver cell damage. This effect was completely prevented by adaptation to hypoxia or administration of ionol and was significantly (by a factor of two) decreased by repeated exposure to short-term stress. The results demonstrate the extreme sensitivity of the liver to stress.

In an additional study, the effects of stress on cholesterol oxidation were studied in bile acids. Each animal was injected with an albumin-stabilized emulsion of 7(n)-α-[^{3}H] cholesterol in a dose of 0.4 ml emulsion with total radioactivity of 13.106 imp/min. This method is based on the finding that in the 7-α-hydroxylation of cholesterol, 1 atom of tritium becomes a component of water, while the amount of ^3H_2O that forms is an indicator of rate of the cholesterol oxidation reaction in the liver microsome system. Urine was collected 2 and 4 hours after treatment and then daily for 8 days. Radioactivity of $^3H_20$ was recorded. In untreated animals ^3H_2O in urine and thus rate of cholesterol peroxidation in bile acids peaked 2 hours after introduction of the marker. Stress undergone immediately before administration of the marker decreased rate of hydroxylation of cholesterol by one-third for the first 1-2 days. Adaptation to hypoxia or administration of ionol prevented the stress-related depression of cholesterol peroxidation in the liver.

Table: Prevention of stress-induced dysproteidemia through adaptation and administration of the antioxidant ionol

Table 2: Concentration of malonic dialdehyde, activity of superoxide dismutases in liver homogenates, and activity of fructose-1-phosphate aldolases in blood serum in response to stress

Figure: The effect of the antioxidant ionol and adaptation to hypoxia on rate of cholesterol oxidation in the liver of rats exposed to stress

P1034(22/89)* Tikhomirov NA, Potapov PP.
Carbohydrates and lipids in the serum and livers of rats repeatedly subjected to hypokinesia.
Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.
23(1): 81-83; 1989.
[8 references; 2 in English]

Metabolism, Lipids, Carbohydrates, Blood, Liver
Rats
Immobilization Cages, Repeated Exposure

Abstract: Subjects in this experiment were 42 experimental and 39 control white rats. Experimental animals were confined in immobilization cages. Rats in groups 1-3 spent 15 days in these cages and then were moved into common cages with free movement possible for 7, 15, and 30 days. At the end of each of these periods, animals were again placed in the immobilization cages and studied on days 7 and 15 of this treatment. Blood serum and liver tissue were studied Concentration of total lipids, cholesterol, and phospholipids were measured. Glycogen was isolated from the liver and the amount measured. Blood sugar was measured.

It was found that the disruptions of lipid metabolism characteristic of response to hypokinesia -- increased cholesterol synthesis and hypercholesterolemia -- did not occur in response to repeated hypokinesia. These changes were lacking even in a group of animals deficient in carbohydrates (second hypokinesia lasting 30 days), while when normally treated animals are immobilized, rapid depletion of glycogen reserves in the liver is one of the main causes of disruption of lipid-cholesterol metabolism. The differences in response to first and second immobilizations depends on duration of intervening recovery period and requires further study.

Table 1: Lipid in blood serum of rats exposed repeatedly to hypokinesia

Table 2: Lipid concentrations in the livers of rats exposed repeatedly to hypokinesia

Table 3; Blood sugar and liver glycogen in rats exposed repeatedly to hypokinesia

MUSCULOSKELETAL SYSTEM

PAPERS:

P992 (22/89) Pozdnyakov OM, Babakova LL, Demorzhi MS.
Changes in the ultrastructure of striated muscle in response to space flight factors.
Byulleten' Eksperimental'noy Biologii i Meditsiny.
1988(12):746-749
(6 references; 2 in English)
Authors Affiliation: Institute of General Pathology and Pathological Physiology, USSR Academy of Health, Moscow

Musculoskeletal System, Striated Muscle, Soleus, Gastrocnemius, Diaphragm
Rats
Space Flight, COSMOS-1667

Abstract: Ultrastructural analysis was performed on portions of the soleus, gastrocnemius, and diaphragm muscles of 6 Wistar rats exposed to space flight for 7 days on board COSMOS-1667 and 7 rats of a vivarium control group. The animals were decapitated 4-8 hours after reentry. Samples were fixed in 4% formaldehyde buffered to pH 7.4 (with an acetate veronal buffer made isoosmotic with sucrose) and stained in a 1% solution of OsO_4, and hardened in araldite. Sections were counterstained and examined through an electron microscope.

Changes were noted in the fibers of the soleus in virtually all structural elements. The most common changes were atrophy of the myofibrils and muscle fibers. The myofibrils were narrow and the spaces between them enlarged, accompanied by unusual fissures, vacuoles, and cavities. Some fibers contained sites where the sarcomere structures were disoriented: zig-zag configuration of the Z-line material, sometimes complete degeneration of the myofilaments, and the formation of light homogeneous small-grained fields with chaotic arrangements of nuclei, small dense mitochondria, fragments of membrane, and myelin-like formations. Some fibers displayed an elevated number of fat globules and inter-myofibril lines of glycogen granules. Along with normal mitochondria, there were giant mitochondria with unusual structures consisting of numerous densely packed christa. Some mitochondria showed swelling of the matrix and fragmentation of the christa. The sarcolasmic reticulum was hyperplastic, exhibiting vacuoles and honey-combed structures. Some muscle fibers had centrally located nuclei. Many showed segregation between the nuclear-sarcoplasmic segments and an increased number of satellite cells at various stages of differentiation. The microcirculatory channels indicated that there were significant changes in microhemodynamics. The arterioles were contracted and the capillaries and venules expanded. The capillary lumen contained compressed erythrocytes, microvesicles with a single layer membrane, and traces of blood plasma. The basilar membrane of the capillaries had widened, become brittle and in some places had broken up. The death of pericyte outgrowths and an increased number of collagen fibrils could be observed. The endotheliocytes of all microvessels were electron dense, active, and contained a large quantity of micropinocytotic vesicles; there were numerous microvilli, veils, and marginal folds. The interstitial substance contained many active fibroblasts, macrophages, and plump cells, partially degranulated.

The gastrocnemius also displayed similar changes in virtually all structural elements, changes were like those described above but these changes were significantly less widespread than in the soleus. In contrast, the diaphragm exhbited only slight myofibril atrophy.

The authors conclude that even relatively brief exposure of animals to weightlessness affects the morphofunctional structure of the muscles to an extent dictated by their antigravity function under normal conditions. Signs of regeneration (segregation of nuclear-sarcoplasmic segments and increase in the number of satellite cells) attest to the reversibility of the structural and functional disruptions induced by weightlessness.

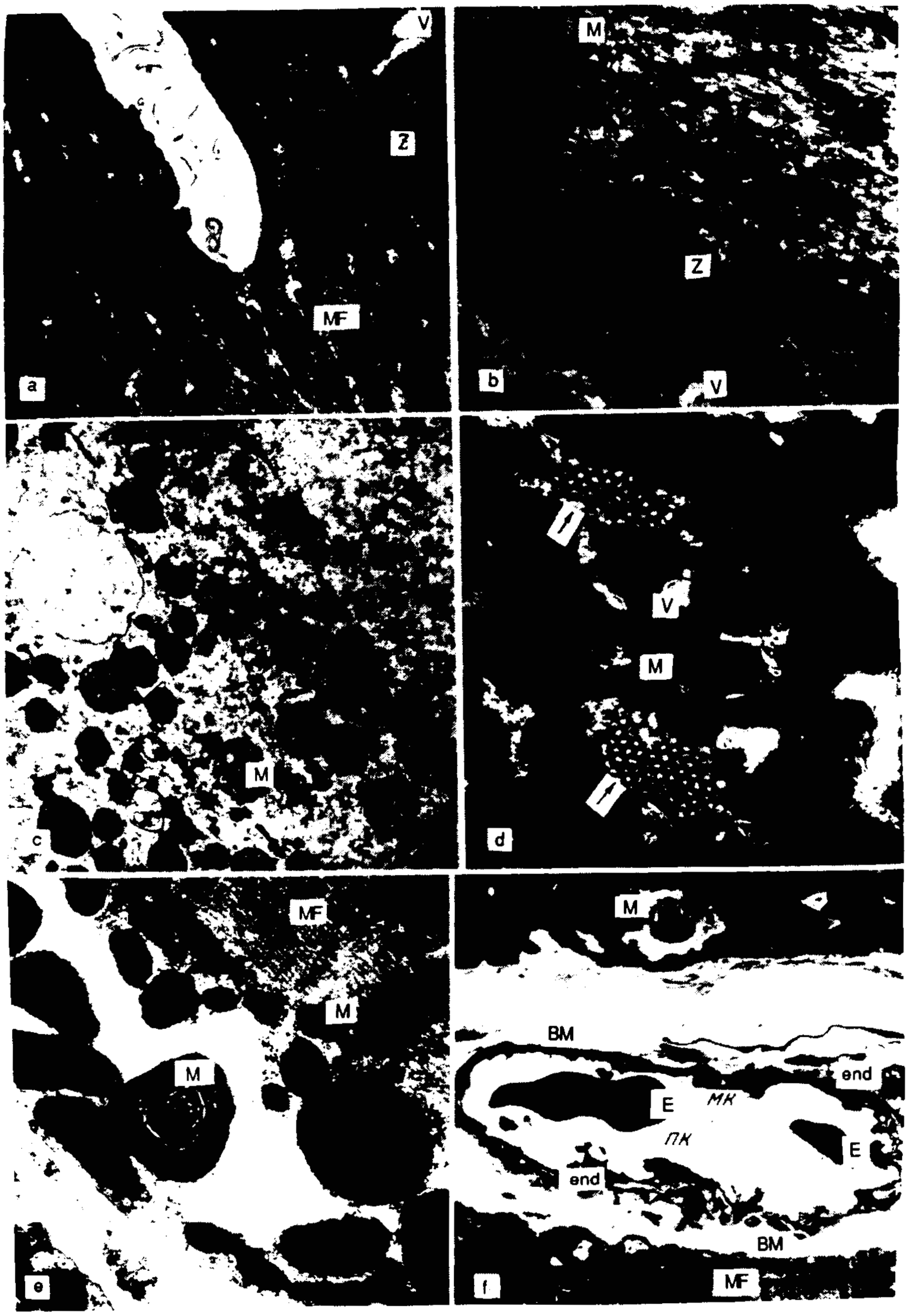


Figure: Changes in the soleus muscle of rats exposed to space flight for 7 days.

a - destruction of myofibrils with formation of cavities filled with membrane fragments. Mag. 20,000. b - local destruction of the structural organization of sarcomeres, and the normal zig-zag configuration of Z-lines. Mag.. 32,000; c - disintegration of myofilaments and formation of light fields filled with homogeneous fine-grained substance, with chaotic arrangement of the mitochondria and membrane fragments. Mag. 20,000. d - hyperplasia of elements of the sarcoplasmic reticulum and formation of honeycomb structures. Mag. 40,000. e - subsarcolemmic accumulation of atypical giant mitochondria. Mag. 32,000; f - capillary lumen with compressed erythrocytes, their ghosts and microvesicles. Endotheliocytes are electron dense, many micropinocytotic vesicles, microhairs, areas of clasmatosis. Basilar membrane is expanded, loosened, with many collagen fibrils, death of pericyte outgrowths. Mag. 17,000.

P1019(22/89) Durnova GN, Vorotnikova YeV, Sakharova ZF, Kaplanskiy AS, Knyazev VM, Dotsenko MA.

Histomorphological study of primate bones after a 14-day period of hypokinesia with head-down tilt.

Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.
23(1): 22-26; 1989.
[13 references; 10 in English]

Musculoskeletal System, Bones, TIbia, Iliac, Lumbar Veretebrae
Primates, Rhesus
Hypokinesia With Head-Down Tilt

Abstract: Subjects in this study were 4 male rhesus monkeys weighing 4 - 4.5 kg. Two monkeys had been exposed to a 14-day period of hypokinesia with head-down tilt (-10°) in a prone position on a special stand; the other two served as controls. Samples of the proximal metaphysis of the tibia bone, crest of the iliac bone, and lumbar vertebrae were fixed in cold 4% paraffin formaldehyde (pH 7.0) for 2 days. After fixation, half of the samples were dehydrated in three changes of acetone at 4° C for 36 hours and embedded in a mixture of methyl- and glycolmetacrylates in a 2:1 ratio. The other half of the samples were decalcified in a 10% solution of EDTA, dehydrated in alcohol, and embedded in histoplast.

Nondecalcified bone was sectioned on a microtome for solid tissues and used for identification of the osteoid and measurement of acid phosphatase activity. The osteoid was stained using a modification of Gomori's method, and acid phosphatase activity was determined through nitrocombination using as a substrate naphthol-AS-BI-phosphate, and as a salt diazonia - strong garnet GBC. Introduction of 1 mM sodium tartrate made it possible to selectively estimate the activity of lysosomal acid phosphatase in osteoclasts, since activity of microsomal isoenzyme of acid phosphatase in osteoblasts is not depressed in the presence of sodium tartrate. The slides of decalcified bone samples were stained with hematoxylin, eosin, picrofuchsin, and methyl green-pyronine.

Histomorphometric analysis was performed using a semiautomated image analyzer. Amount of spongy bone was estimated on the basis of volume (T V). and surface density (S_V) of trabeculae, mean density (MTPD) and mean thickness (MTPT) of trabeculae, mean distance between trabeculae (MTOS), and volume of calcified bone tissue trabeculae (V_{calcif}). Rate of new growth of bone tissue in the primary spongiosa was evaluated by counting the number of osteoblasts in 1 mm^3 spongiosa, while an index of osteoblast activity was computed by counting the number of high, moderate, and low activity osteoblasts; multiplying them by a factor of 3, 2, and 1, respectively; then dividing by total numberof osteoblasts. New bone growth in secondary spongiosa was estimated on the basis of volume and surface of the osteoid and the osteoid index. Parameters selected to show bone tissue resorption were: number of osteoclasts per 1 mm^3 spongiosa, 1 mm^3 bone trabeculae, and 1 mm^2 surface of bone trabeculae. Osteoblasts were counted in sections of stained decalcified bone, and osteoclasts counted in sections of nondecalcified bone after acid phophatase activity had been measured.

Two weeks of exposure to hypokinesia with head-down tilt decreased the quantity of spongy bone in the proximal metaphysis of the tibia bones in both monkeys, as indicated by decreased volume of primary spongiosa and the decreased density of trabeculae. The thickness of trabeculae was unaltered, but the distance between them increased. In the same bones, only a slight decrease was noted in trabeculae and calcified bone in the secondary spongiosa. There were decreases in the number and functional activity of osteoblasts in the area of the primary spongiosa, suggesting inhibition of new formations. In the secondary spongiosa, there were initial signs of

a similar inhibition. Morphological signs of increased resorption were less marked and occurred mainly in the area of the primary spongiosa. Reduction of iliac bone tissue was noted in both primates in both the primary and secondary spongiosa. This decrease was manifested by decreases in volume and surface density of the spongiosa, density and thickness of trabeculae, volume of calcified tissue, and increased intertrabecular distance. There was also inhibition of new formation, as manifested by decrease in number and activity index of osteoblasts in the primary spongiosa and decrease in osteoid volume and surface area in the secondary spongiosa. Number of osteoclasts per unit volume of trabeculae increased only in the primary spongiosa.

The primary spongiosa was not clearly delineated in the lumbar vertebrae of either experimental or control animals and thus only the secondary spongiosa was analyzed histomorphologically. Only one experimental animal showed the initial signs of reduction of spongy bone: calcified tissue and increased intertrabecular distance. Parameters of new growth rate decreased in both animals. Rate of resorption of bone tissue increased in both animals.

The authors argue that decreased number and functional activity of osteoblasts in the primary spongiosa, and decreased number of osteoids in the secondary spongiosa of the bones studied demonstrate that inhibition of bone formation is an important response to hypokinesia with head-down tilt. However, this study failed to strongly confirm that resorption of spongy bones increased, as other authors have observed in response to the same treatments.

Table 1: Data from histomorphometric analysis of spongy substance in the proximal metaphysis of the tibia bones

Table 2: Data from histomorphometric analysis of spongy substance in the proximal metaphysis of the iliac bones

Table 3: Data from histomorphometric analysis of spongy substance in the proximal metaphysis of the lumbar vertebrae

Figure 1: Osteoid in bone trabeculae of the iliac bone of a primate
Stained according to Gomori in Villanueva's modification. Ob.10, oc.7.

Figure 2: Osteoclasts with high activity of acid phosphatase in the primary spongiosa of the iliac bone in a primate
Simultaneous nitrogen-combining reaction. Ob.16, oc. 7.

P1020(22/89)* Shvets VN, Pankova AS.
The effects of α-hydroxydimethyl-γ-aminopropylidene bisphosphonate on bone tissue of rats undergoing hypokinesia.
Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.
23(1):27-31; 1989.
[17 references; 13 in English]

Musculoskeletal System, Bone Tissue, Osteoporosis
Rats
Hypokinesia, Immobilization; Biphosphonates

Abstract: The goal of this study was to investigate the possibility of preventing osteoporosis in rats undergoing hypokinesia through the use of α-hydroxydimethyl-γ-aminopropylidene bisphosphonate (HDAB). Subjects were male Wistar rats. In the first experiment, eight groups of subjects were either exposed or not exposed to hypokinesia for 35 days, and received either no HDAB, 0.005 mg/kg HDAB subcutaneously daily for 35 days, or 0.01 mg/kg of the same substance for the same period. Hypokinesia was produced by placing the animals in immobilization cages. (See Table 1). Each group contained 10 rats. After 35 days had elapsed, the animals were sacrificed and the bones of the legs, trunk, and pelvis were fixed in 10% calcium formol, decalcified in 6% trichloroacetic acid, and poured into histoplast. Histological sections 5-7μm were stained with hematoxylene and eosin toluidine blue. In a second experiment, 5 mg/kg HDAB was injected daily into rats for 10 days. One day after the last dose, some of the animals were sacrificed. The remaining rats were either subjected to 35 days of hypokinesia, or allowed freedom of movement. At the end of the experimental period bones of the legs, trunk, and pelvis were isolated and the material subjected to histological studies as described above. Again there were 10 animals in each group. The volume density of spongy bone, linear parameters of cartilage layer, and the number of osteoblasts and osteoclasts in the area of the primary spongiosa in a visual field of 0.36 mm^2 were also measured. Statistical significance was tested using Student's t.

Hypokinesia alone led to decreased mass of spongy bone in various parts of the skeleton, with the exception of the sternum. HDAB administered daily in a dose of 0.005 or 0.01 mg/kg during 35 days of hypokinesia prevented bone loss in all the bones studied. Effects were seen in total bone and in the high metabolic portion of spongy bone. Injection of HDAB in subjects without restricted movement led to increased bone mass by a factor of 1.1 — 2. The drug did not affect rate of bone growth, as indicated by the width of the epiphysial growth layer, which decreased during hypokinesia and was unaffected by HDAB. Effects of hypokinesia and HDAB on cartilage were similar to those on spongy bone. Number of osteoblasts decreased by more than a factor of two during hypokinesia and were unchanged by HDAB. Number of osteoclasts increased to normal levels in hypokinetic rats receiving HDAB. Control rats receiving the drug showed increased osteoclasts and unaltered osteoblasts. The authors conclude that daily administration of HDAB prevents osteoporosis due to hypokinesia. The relative effectiveness of low doses suggests that this compound accumulated in the bone and should therefore have prolonged effects; thus preliminary administration of high doses should also prevent this condition.

The results of experiment 2 indicate that an injection of 5 mg/kg of HDAB for 10 days prior to hypokinesia increased mass of spongy bone in the tibia and iliac bones, but not the bones of the trunk. When animals receiving this treatment were placed in immobilization cages for 35 days, the drug not only prevented osteoporosis but actually increased bone mass beyond control levels. When animals were exposed to hypokinesia without the drug, the volume of fatty tissue in the marrow cavity of the metaphysis of long bones and bodies of the vertebrae, sternum and iliac increased by a factor of 4-6. Animals in all other groups showed normal values of this parameters. Preliminary injection of HDAB did not prevent decreases in the epiphysial growth layer. Administration of HDAB led to decreased numbers of osteoblasts in the tibia and iliac

bones. During subsequent exposure to hypokinesia or free movement conditions, these parameters remained depressed Bones of the trunk remained at normal levels. Osteoclasts were not initially affected by HDAB, decreased during hypokinesia alone, and increased to normal levels in animals receiving both treatments. Animals receiving the drug and then allowed free movement had elevated levels of osteoclasts. No side effects were noted in either experiment. The authors argue that the effects of the drug must be due to modification of the relationship between bone formation and bone absorption. HDAB is hypothesized to alter sensitivity of bone cells to endogenous and exogenous osteogenesis factors. The mechanism is supposed to involve the influence of bisphosphonate on the structural and functional characteristics of the cells resulting from disruption of calcium metabolism within the cells and in the intercellular interstices. Because of its effectiveness and lack of side effects, the drug is considered very promising in preventing disuse osteoporosis.

Table 1: Some parameters of growth of the tibia in response to administration of HDAB during hypokinesia

Table 2: Number of bone cells in the area of the primary spongiosa (in an area 0.36 mm) of various bones

Condition	Tibia		Vertebra		Sternum		Iliac	
	osteo-blasts	osteo-clasts	osteo-blasts	osteo-clasts	osteo-blasts	osteo-clasts	osteo-blasts	osteo-clasts
1.Placebo, 10 days	130±7.6	20±1.4	45±5.0	12±0.9	36±5.8	9±0.8	101±10	22±2.7
2.HDAB (5 mg/kg)10 days	70±8.0*	26±2.4	32±8.1	17±0.8*	24±6.8	12±1.0	65±8*	21±1.2
3.. Placebo (10 days) + hypokinesia 35 days	52±4.0*	10±1.2*	18±1.6*	6±1.0*	11±1 8*	4±0.4*	20±2.6*	5±1.2*
4.HDAB (5 mg/kg) 10 days + hypokinesia 35 days	60±7.5*	19±1.4	37±4.3	16±1.3	22±4.0*	9±0.9	46±6.0	15±1.6
5. Placebo 10 days +free movement 35 days	112±14.0	20±2.0	46±7.0	13±1.4	38±6.0	11±1.2	90±4.0	19±3.0
6. HDAB (5 mg/kg) 10 days+ free movement 35 days	50±4.0*	32±2.0	46±6.0	18±1.4*	41±8.0	19±2.0*	30±2.0*	31±1.5*

*Statistically significant difference from Group 1.

Figure 1: Total mass of spongy bone in metaphysis (a) in the area of the primary spongiosa (b), tibia, in the body of the vertebra (c), sternum (d) and iliac bone (e) of rats receiving HDAB during hypokinesia

Figure 2: Mass of spongy bone in the metaphysis (a) and area of primary spongiosa (b) of the tibia bone of rats receiving HDAB before the experimental period

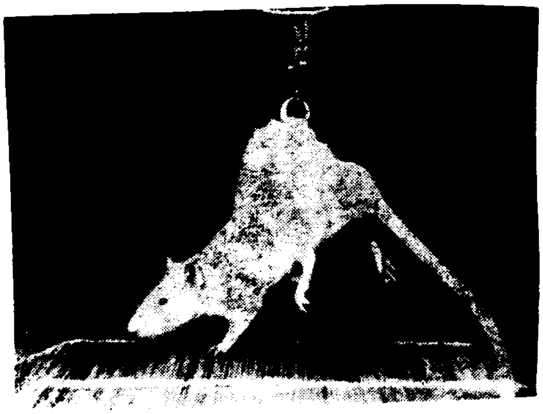
Figure 3: Mass of spongy bone found in the area of the spongiosa of the vertebra (a), Sternum (b) and iliac bone (c) of rats receiving HDAB before the experimental period

P1031(22/89) Kuznetsov SL, Talis VL.
Simulating the physiological effects of weightlessness by the method of "head-down suspension" of small laboratory animals.
Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.
23(1):74-76; 1989.
[17 references; 10 in English]

Musculosketelal System, Femur, Atrophy; Enzymology, Muscle Enzymes; Psychology, Behavioral Responses
Rats
Equipment and Instrumentation, Weightlessness Model, Suspension

Abstract: This paper describes tests of the physiological effects of a new method of head-down suspension. This method uses a strip of porous rubber, 5-6 cm^2, to which a loop is attached that is glued to the shaved back of the rat with biologically reactive glue. This method is claimed to have fewer adverse "side effects" than the previous method of tail suspension. In the test male Wistar rats (n not specified) were divided into two groups, a control and a group of suspended animals. On day 14 and 21 of suspension, some of the animals were sacrificed and their femurs were analyzed morphologically. Samples of skeletal muscle were rapidly frozen in liquid nitrogen and a series of sections 10 μm in width were obtained. Activity of Ca-dependent ATPase myosin, NADH-tetrazole reductase (NADH-TR), succinate dehydrogenase (SDH), lactate dehydrogenase (LDH), and hydroxybutyrate dehydrogenase (HBDH) were measured Concentrations of glycogen, RNA, and total protein were also measured, as were cross sections of muscle fibers. Other animals were tested on a treadmill and for response to pain, delivered by a shock of 0.5-2 mA for 5 seconds, on days 14 and 21 of suspension.

The new form of suspension permitted the animals to manipulate to groom themselves without damage to their skin, but kept ordinary movement to a minimum. Only one animal succeeded in ripping off the device. Behavioral reactions of experimental animals were virtually identical to those of controls, and no experimental neuroses were noted. Performance on physiological tests was normal. Weight gain was only slightly less for experimental than for control animals. However, signs of atrophy were noted in the muscle fibers of the femur, which were especially pronounced on day 21, when signs of atrophy had decreased and were virtually absent in type IIB fast-twitch "glycolytic fibers." Rate of physiological regeneration, as revealed by RNA and total protein levels, was virtually unchanged in type I slow-twitch fibers. However, on day 21 there was some decrease in RNA concentration in types IIA and IIB fibers, suggesting inhibition of protein synthesis. Total protein levels were somewhat elevated, perhaps as a result of decreased degradation. All fibers showed elevation of NADH-TR on day 14, followed by a decrease on day 21. A decrease in HBDH was evidently associated with lower utilization of lipids under conditions of hypokinesia. Decreased SDH activity in type I fibers was fiber specific and was evidently associated with disruption of circulation during the initial experimental period. This explanation is confirmed by increase in SDH by day 21. LDH was elevated in all fibers on day 21, suggesting that metabolism failed to normalize fully. On day 21, glycogen had accumulated in all fibers, a phenomenon also noted in response to weightlessness, but not present in other suspension models. The authors recommend this model as an improvement over previous models for simulating effects of weightlessness.



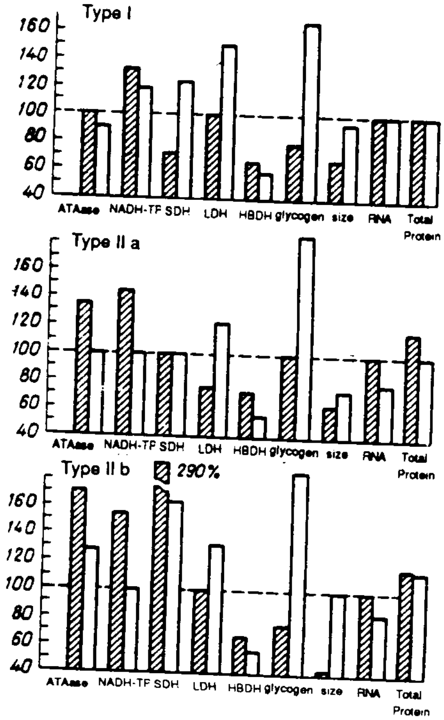


Figure 1: New method of restraint of rats through "head-down suspension"

Figure 3: Change in activity of ATPases myosin, NADH-TR, SDH, LDH, and HBDH, concentration of glycogen, RNA, and total protein in various types of skeletal muscle fibers of rats after suspension varying in duration

Hatched bars - 14 days, white bars - 21 days.

Figure 2: Relative body weight increase of animals subjected to new method of suspension

P1035(22/89)* Volozhin AI, Amel'kina GV, Golubev SN, Komnova ZD, Remizov SM, Bakulin AV.

Changes in the jaw bones of rats after a 7-day flight on COSMOS-1667.

Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.
23(1): 83-86.; 1989.
[9 references; 4 in English]

Musculoskeletal System, Jaw Bones
Rats
Space Flight, COSMOS-1667

Abstract: Studies were performed on 28 male Wistar rats. The animals were divided into 4 groups with 7 members each. Group 1 was a vivarium control; group 2 was the flight group; 3 was a second vivarium control; and 4 was a synchronous ground control group. Duration of the flight and synchronous simulation was 7 days. In group 4, all space flight factors were simulated with the exception of weightlessness. After the 7-day period, the animals were sacrificed and their upper and lower jaws isolated and fixed in a 10% solution of neutral formalin. Decalcification was performed in a 25% solution of EDTA. The material was poured in celloidin and stained with hematoxylin, eosin, and picrofuchsin. The microhardness of bone tissue was measured on sagittal sections of the upper jaw, enclosed in plastic. Three areas were studied: near the crest of the alveolar process, in its middle section, and in the body of the jaw. Ten measurements were made in each area with a loading of 20 gram-force.

The CO_3/PO_4 ratio was measured using infrared spectroscopy in 9 samples from the four groups; these data were not processed statistically. A selective analysis was made of the anions comprising the apatite. The apatite portion was removed at low-temperature by soaking bone fragments in 30% hydrogen peroxide, with a titrated solution of ammonia until slightly alkaline pH values were attained. After pulverization on a vibration mill the samples were compressed along with KBr. CO_3/PO_4 ratio was estimated on the basis of peaks at 1650 and 1050 cm^{-1}.

Visual examination of the histological preparations revealed small differences in the animals in the two experimental groups compared to the vivarium controls. These groups showed slight atrophy of the gingival papillae in the area of the incisors and molars of the lower jaw with vegetation of the epithelium in the underlying connective tissue and hyperemia of the periodontal vasculature. The contours of the bone alveoli were less even than in the control due to recesses in the bone tissue. Numerous basophilic lines of adhesion were observable in the alveoli. In the area of the tooth socket bottoms, places in the osteocytic cavities were either empty or filled with eosinophilic masses. Thus, both the flight and synchronous control groups showed similar effects, involving hyperemia of vasculature, congestion in the interdental papillae and some enhancement of bone tissue resorption.

These changes were accompanied by changes in the biomechanical characteristics of the bone. Both vivarium control groups showed similar patterns of microhardness in all areas tested. The bone in the alveolar process was less mineralized than that in the body of the jaw. In both the flight and synchronous control groups, microhardness was diminished in all three areas. Thus, changes are attributed to factors other than weightlessness. Space flight was associated with marked decrease (by a factor of 1.5-2) of the CO_3/PO_4 ratio compared with the vivarium control, suggesting a specific effect of weightlessness. This ratio was somewhat higher than control in the synchronous group. CO_3 anions have an inhibiting effect on the growth of apatite crystals. Deficits in CO_3 anions occurring in space thus could have serious consequences, leading to defects in the matrix, and increased risk of microfissures, weakening the bone.

Table: Effect of 7-days of space flight on microhardness (in kgf/mm^2) of various areas of the upper jaw

Group	Area: Crest of the alveolar process	Area: Middle of the alveolar process	Area: Body of the jaw
1 (vivarium)	67.2±0.7	67.3±0.8	81.1±0.7
2 (flight)	55.1±1.4*	57.2±1.2*	59.4±1.1*
3 (vivarium)	69.2±1.0	70.9±1.2	81.6±1.2
4.(synchronous)	48.2±0.9*	48.4±1.0***	50.7±1.2*

* — $p < 0.001$ compared to vivarium control; *** - no key provided

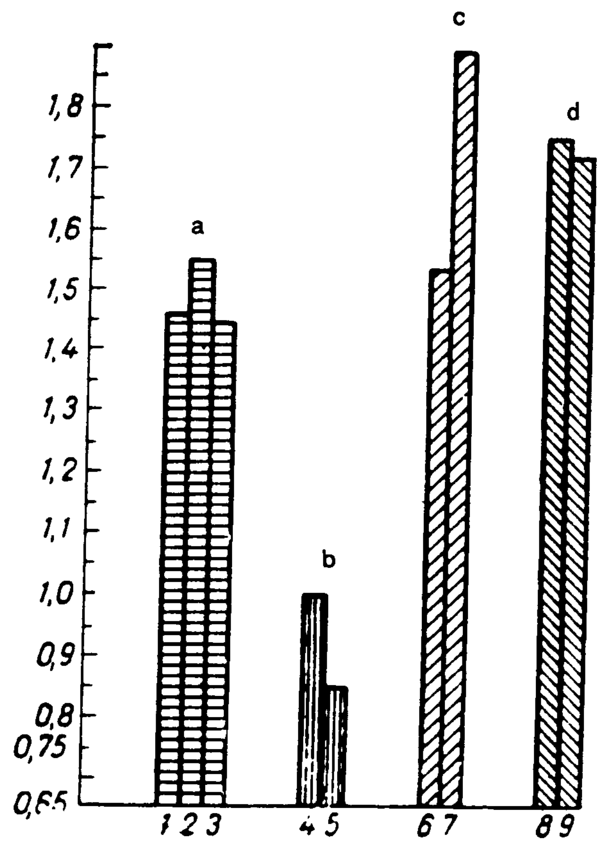


Figure 1: Effect of space flight on the CO_3/PO_4 ratio in mineralized tissues of the lower jaw

Abscissa — number of samples; ordinate — CO_3/PO_4 ratio, a, b, c, d, — groups 1, 2, 3, and 4, respectively

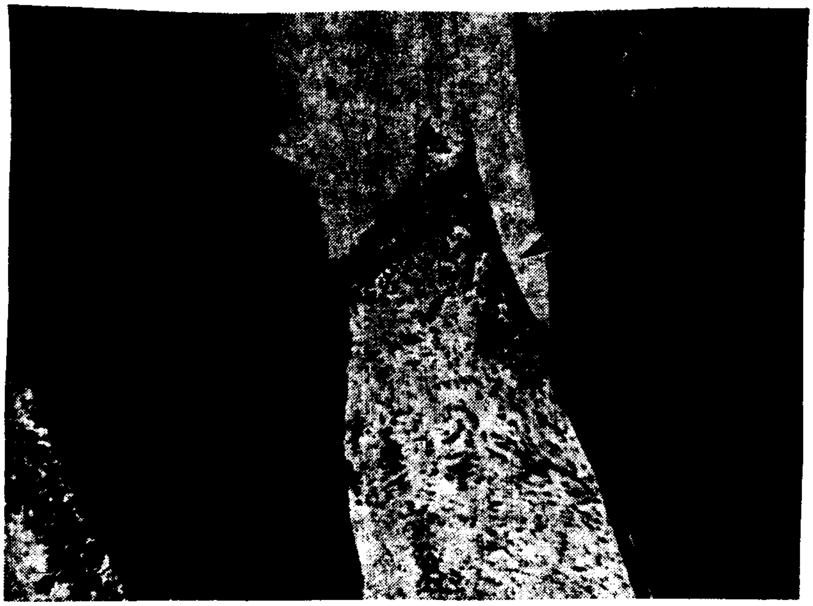


Figure 2: Gingival papillae of a molar of the lower jaw of rats after 7 days of space flight. Atrophy and epithelial vegetation along the molar cement (arrow). Stained with hematoxylin and eosin (here and in figure 3, 4), Mag. 80.

Figure 3: Periodontium in the area of an incisor of a rat after a 7-day space flight Hyperemic vasculature (arrow). Mag. 100 (here and in Figure 4).

Figure 4: Bone tissue of the alveolar cavity of the molar of a rat after a 7-day space flight. Numerous lines of adhesion (arrows) can be seen.

NEUROPHYSIOLOGY

PAPERS:

P1026(22/89)* Razinkin SM, Kordenko AN, Ushakov IB, Dukhovich VM.
Some parameters of brain metabolism under exposure to hypoxia and overheating.
Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.
23(1): 51-56; 1989.
(13 references; 2 in English)

Neurophysiology, Brain; Metabolism, Enzyme Activity; Body Fluids, Brain Hydration
Rats, Female
Adaptation, Hypoxia, Overheating, Long-term; Radiobiology, Gamma Irradiation

Abstract: The goal of this experiment was to investigate endurance of animals exposed to hypoxia, heat, and radiation as a function of duration of previous long-term exposure to hypoxia and heat. The major focus was on functional and metabolic changes in the central nervous system. A total of 224 outbred white female rats served as subjects. Hypoxia was created in a barochamber at an altitude equivalent of 6500 m, with exposure duration of 120 minutes. Rate of ascent and descent was 1000 m/min. To induce adaptation to heat, animals were placed in a thermal chamber with air and wall temperatures of 35-36° for 180 minutes daily. Various types of adaptation were studied and material was taken for histo- and biochemical studies the day after the training session on days 3, 7, 14, and 21.

Hypoxia tolerance was measured by raising the rats to an altitude equivalent of 1200 m at a rate of 1000 m/min. The animals' tolerance was estimated on the basis of time elapsed from the start of air pressure changes to occurrence of a second gasping breath. When this occurred the animals were rapidly recompressed and 5 hours later sacrificed for histological and biochemical analyses. Preliminary studies had shown that 5 hours was the minimum time required for most histochemical brain characteristics to return to normal in nonadapted animals. Thermal tolerance was measured in the thermal chamber by raising the temperature to 55 - 56°C. The parameter measured was time between beginning of exposure until the animal's breathing stopped. Because the animals died, no sample tissue was taken for histochemical analysis The tolerance of an animal's central nervous system to radiation was evaluated from abnormal neurological symptoms occurring after cranocaudal γ-irradiation (^{60}Co at a dose of 62.5 Gy presented at a rate of 45.83 Gy/sec). The animal's ability to endure this exposure was estimated on the basis of frequency and duration of general tremor, its tendency to run in circles, hyperactivity, opisthotonus, and convulsions. When 100 minutes had elapsed after irradiation terminated, tissue for histo-biochemical analyses was taken. This period had been found to be the maximum one during which no significant histochemical changes are observed in the brains of unadapted animals. Metabolism was studied in samples of the frontal lobe of the cerebrum, which had been quick-frozen. Sections 15 μm thick were treated by tetrazole reductase methods to identify activity of key glycolysis and Krebs cycle enzymes — lactate dehydrogenase (LDH) and succinate dehydrogenase (SDH). In addition the nitrogen-combining method was used to measure activity of alkaline phosphomonoesterase (AP), an enzyme important in active transport in the endothelium of the microcirculatory tract. Activity of dehydrogenase was evaluated spectrometrically using the two-wave method. In analyzing AP activity, the surface area of positively reacting endothelium was measured. The state of hydration of four areas of the brain — cerebellum, brain stem, and frontal and temporal lobes— was evaluated using the dehydration method. Results were subjected to t-tests and the Wilcoxon-Mann-Whitney test for paired data.

On day 4 after hypoxia, there was significant decrease in activity of both dehydrogenases in the temporal lobe of nonpreadapted animals. Subsequently the enzymes tended to normalize, although SDH remained somewhat elevated and LDH and AP were somewhat depressed. Preadaptation to hypoxia increased hypoxic tolerance, especially after 14 days of pretraining. Under these conditions the metabolic response of the brain to acute hypoxia altered. After 3 sessions of hypoxia, preadaptation responses were analogous to those obtained in animals that had no pretraining. The significant increase in hypoxia tolerance occurring after 7 and 14 pretraining sessions was accompanied by a sharp decrease in SDH and AP activity in the cortex and no changes in LDH in response to the hypoxic test. This result suggests that 5 hours after exposure to acute hypoxia preadapted animals show signs of inhibited oxygenation from blood to brain tissue and decreased oxygen-dependent oxygenation in nerve cells of the brain. After 21 days of preadaptation, acute hypoxia evoked an increase in the activity of redox enzymes in neural tissue, while activity of AP remained low in brain vasculature. These same animals showed smaller increases in tolerance than those preadapted for a shorter period. Adaptation to hypoxia decreased radiation tolerance and altered enzyme activity. After 7 days of preadaptation, irradiation led to a significant increase (compared to nonirradiated preadapted rats) in the stereometric AP parameters, which was manifest to a lesser extent in animals adapted for 15 days. The animals were apparently sensitized to radiation since in the norm such symptoms occur only after lethal doses. After 21 hypoxia sessions, the reaction of endothelial AP to gamma irradiation altered, and decreases in tissue oxygenation were demonstrated, along with an increase in radiation tolerance. Heat tolerance increased after the first four hypoxia adaptation sessions and remained at that level throughout the rest of the period. No associations were noted between heat tolerance and altered enzyme activity.

Enzyme responses in the brain after preadaptation to heat were similar to those occurring in response to hypoxia. The decrease in dehydrogenase activity was less pronounced after the initial sessions of adaptation, but after 14 preexposures to heat, the decrease in AP activity was greater. Heat preadaptation affected tolerance of hypoxia, heat, and radiation in a fashion very similar to hypoxia preadaptation.

One hundred minutes after exposure to radiation, the cerebellum was dehydrated; while hypoxia was followed by dehydration of the frontal lobes and brain stem. Preadaptation to hypoxia only affected hydration of the cerebellum after 3 sessions. Preadaptation to hypoxia followed by exposure to radiation was associated with increased dehdyration in all structures after 3 and 21 adaptation sessions. Preadaptation to hypoxia followed by acute hypoxia led to marked dehdyration after 3 and 21 sessions, but these effects were much less marked or even opposite in direction after 7 and 14 sessions. Preadaptation to heat led to very similar changes in brain dehdyration after hypoxia and irradiation.

The authors argue that there are at least three phases in preadaptation effects on tolerance — as exemplified by resutls on day 4, day 8-15, and day 22. The similarity in brain hydration with and without the loading tests (acute exposure to radiation or hypoxia) suggests a common response during adaptation sessions and tests. Adaptation to both hypoxia and heat is associated with increased tolerance to these factors and decreased tolerance for radiation. Along with generalized response, there is also a specific response, since adaptation to hypoxia increases hypoxia tolerance the most, and the analogous phenomenon occurs with heat. Patterns of change in all the parameters studied show definite phases. Tolerance increases after 8-15 adaptation sessions and decreases after 21. That the animals developed a high tolerance to hypoxia during preadaptation is correlated with decreased aerobic oxygenation in nerve cells and enzyme-dependent transport in the endothelium of brain vasculature. Decreases in radiation tolerance after preadaptation to the two factors may be associated with the signs of increased permeability of the blood-brain barrier, as reflected in changes of hydration of brain structures.

Figure 1: Changes in activity of succinate dehydrognease, lactate dehydrogenase and alkaline phosphomonoesterase, in the brain during exposure to hypoxia and heat, 5 hours after exposure to hypoxia, and heat, and 100 minutes after irradiation

Figure 2: Changes in tolerance of hypoxia, radiation, and heat after adaptation to hypoxia and heat

NUTRITION

PAPER:

P1027(22/89)* Davydova NA, Belakovskiy MS, Ushakov AS.
Activity of neurohumoral regulation systems and its adjustment under arid environmental conditions.
Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.
23(1): 56-61; 1989.
(14 references; none in English)

Neurophysiology, Sympathetic Adrenal System
Humans, Expedition Members, Male
Adaptation, Extreme Factors, Desert; Nutrition, Diet Supplements

Abstract: This study investigated dietary correction of responses of the sympathetic adrenal system (SAS) to an expedition to an arid area. Subjects were 7 male members of an expedition to a hot dry area, aged 25-35. Subjects were not acclimated to the climate, which during the 23-day expedition period had a mean temperature of 33.8° C, (36-37° during the final stage) with ground temperature of 37°, relative humidity was 44.6%. Subjects ate a standard balanced diet and had free access to water. Baseline measurements were taken twice and then the subjects completed a 2-day walk (50 km) across the desert, after which they were medically examined. Subsequently, 4 of the 7 individuals (group 1) were given daily nutritional supplements containing 50 g protein concentrate (whey) and a new multivitamin. The remaining expedition members (group 2) received no supplement. Activity of the sympathetic adrenal system was estimated on the basis of concentration of adrenaline (A) and noradrenaline (NA) in blood, and A, NA, dopamine (DA), metanephrine (MN), normetanephrine (NMN), and DOPA in urine using fluorometric methods. Vanillylmandelic (VMA) and homovanillic acids (HVA) (not stated whether sampled from blood or urine) were measured using thin layer chromatography. Ratios among the different catecholamines were computed.

The second baseline measurement revealed increased renal A, which was evidently a response to altered environmental conditions. The acute period of adaptation was marked by a pronounced increase in A and NA into blood and increased renal excretion of A, NA, DA, DOPA, MN, NMN, VMA, and HVA in all subjects. Changes in ratios can be seen in figures 1 and 2. The authors attribute changes to thermal stress that triggered adaptive mechanisms in the SAS. The pattern of changes was identical for all expedition members.

During the readaptation period, blood concentrations of A and NA continued to be elevated in both groups until day 3; renal excretion of A was below the previous level in all subjects. Excretion of NA, DOPA, NMN, HVA, and VMA exceeded all previous values, while DA excretion was normal. Effects were more pronounced in subjects in group 2 (no nutritional supplements). The A/NA ratio was lower in group 1 than in group 2 subjects, but was still above baseline. NA was elevated and DA depressed in both groups, but to a greater extent in group 2. The relative activity of A methylation (MN/A) was depressed in both groups, NA was also depressed, but reached baseline in group 1. The relative activity of DA inactivation (HVA/DA) was markedly elevated, while the process of catecholamine deamination (VMA/MN+NMN) was depressed. Overall, the total secretory activity of the SAS was higher in group 2 subjects; however, the ratio of this activity to the free forms was higher in the first group, suggesting greater activity of adaptive mechanisms. The authors conclude that nutritional supplements are a promising countermeasure against stress reactions evoked by extreme environmental conditions.

Table: Results of study of catecholamines and their metabolites in expedition members

Flow Chart 1: Hormonal-humoral reactions to exposure to high environmental temperature

Flow Chart 2: Physiological reactions to high environmental temperature

Flow Chart 3: Adaptation to high temperature

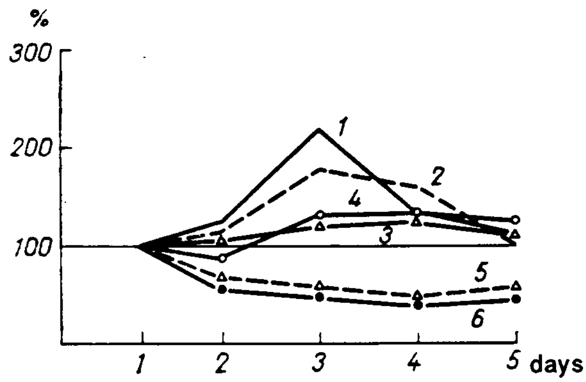


Figure 1: Parameters of relative metabolic activity of catecholamines in subjects of group 1 (1, 3, and 5) and 2 (2, 4, and 6)

Data on mean renal secretion. Baseline 1 measurements are taken as 100%.

1 and 2 - A/NA; 3 and 4 - NA/DA; 5 and 6 - DA/DOPA;

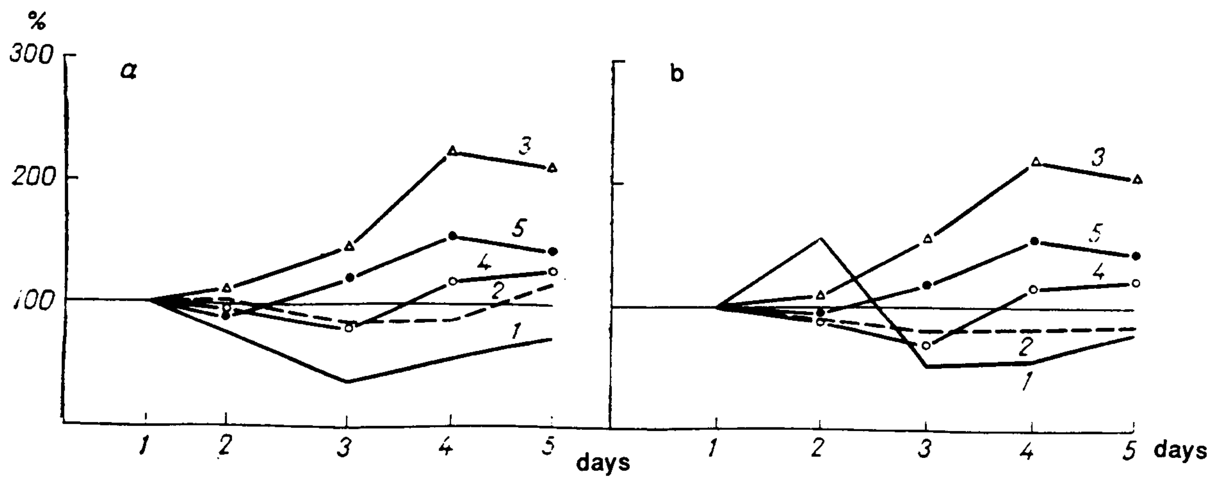


Figure 2: Parameters of relative activity of catecholamine metabolism in members of groups 1 (a) and 2 (b)

1 - MN/A; 2 - NMN/NA; 3 - HVA/DA; 4 - VMA/MN+NMN

OPERATIONAL MEDICINE

PAPERS:

P985(22/89)* Barer AS, Lakota NG, Ostrovskaya GZ, Shashkov VS.
Pharmacological correction of the effects of cold on humans.
Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.
22(6): 66-73; 1988.
(15 references; 4 in English)

Operational Medicine, Hypothermia
Humans
Pharmacological Countermeasures

Abstract: The goal of this work was to investigate how neurotrophic substances correct human thermal status during exposure to acute cold. Substances studied were sydnocarb (N-phenylcarbamoyl-3-(beta-phenylisopropyl)-sydnonimine; phenamine (benzadrine sulfate), ephedrine (ephedrine hydrochloride), strychnine, indopan (an indolic analog of phenamine), lagochilus (the plant intoxicant *lagochilus)*, and glutamic acid. Four conditions were run; in the first, subjects (no n or population specification) spent 6-8 hours in a thermal chamber at a temperature of -20°C while wearing a thermal protective suit with heat resistance of 2.5 KLO; subjects were offered the opportunity to work out on bicycle ergometers to keep themselves warm. Mean work performed was 40-70 W. Drugs tested were: phenamine, 0.01 g, once in hour 3; sydnocarb, 0.01 g, twice in hours 2 and 4; indopan, 0.005 g, twice in hours 3 and 6; glutamic acid, O.5 g, before treatment + lagochilus, 100 ml extract, in hour 3 + 0.025 ephedrine in hour 6. In the second condition, subjects spent 12 hours in a pool of water (-6° - 15°) wearing a waterproof suit over a thermal protective suit. Subjects were maintained in a floating position by means of an air layer inside their suits and were instructed to maintain muscle relaxation. Drugs used were 0.02 g sydnocarb + 0.5 g glutamic acid three times at 3-hour intervals starting 1.5 hours after experiment began); 0.05 g ephedrine + 0.001 g strychnine + 0.5 g glutamic acid twice with an interval of 4 hours (first dose 1.5 hours after experiment began). No drug control groups were run in conditions 1 and 2. The third condition was like the second, but was directed at determining maximum endurance. This condition lasted up to 18 hours. Drugs used were: placebo, 5 doses every 3 hours; 0.03 g sydnocarb, 5 doses every 3 hours, first dose right before immersion. The fourth condition was similar to the third, except that subjects were allowed to engage in vigorous swimming if they desired. This condition lasted up to 20 hours and used 0.03 g sydnocarb + 0.5 g glutamic acid, 5 doses every 3 hours.

In all conditions, the subjects were removed from treatment upon request or on onset of clinical symptoms of hypothermia. Before treatment each subject was tested individually for thermal tolerance. A total of 48 subjects were used. Subjects were kept under continuous medical observation and their verbal comments were recorded. In addition EKG, skin temperature (at 7 points), gas exchange, and rectal temperature were recorded. Expired gas was collected for 1 minute every 2 hours for the first 6 hours and subsequently every hour. Oxygen consumption was computed. A total of 4 to 8 subjects were used in each condition.

In condition 1, control subjects reported feeling very cold after 2 hours of exposure; exercise did not warm them up. Rectal temperature and skin temperature decreased progressively. Energy expenditure increased. Phenamine appreciably improved thermal comfort starting 30 minutes after administration and lasting for 1.5 to 2 hours. Subsequently, symptoms of cold stress were actually worse than those of control subjects; exercise did not help. Objectively. phenamine improved rectal and skin temperature somewhat compared to control, but it increased energy expenditure by a factor of 2 and significantly increased heart rate. Indopan

raised rectal temperature and decreased skin temperature. Subjects reported no improvement or a worsened state with unpleasant side effects. The combination of ephedrine, glutamic acid, and *lagochilus*, did not improve subjects' self reports; decrease in rectal temperature was somewhat inhibited, and energy consumption decreased, and skin temperature was rather high. All subjects reported improvements after taking sydnocarb. Rectal and skin temperatures were unaffected; heart rate was depressed and energy expended on the bicycle ergometer was lower than in any other condition.

In the second condition, control subjects reported thermal discomfort; at 4-5 hours of exposure their hands and feet began to freeze and they started to shiver; severe exhaustion occurred at 8 hours, accompanied by bradycardia and muscle cramps. Subjects expressed the desire for active motion. In general, oxygen consumption increased. All subjects noted a positive effect from taking sydnocarb combined with glutamic acid. Objective parameters stabilized at a level closer to normal than in the group not receiving drugs. Ephedrine + strychnine + glutamic acid was not effective in preventing the adverse effects of cold.

In the third experiment, under conditions of inactivity sydnocarb and sydnocarb combined with glutamic acid increased duration of subjects' endurance of cold by 2-6 hours. When syndocarb was used, in no case was the experiment terminated due to onset of critical temperatures or other symptoms. Beginning in hour 4 , rectal temperature was higher than under placebo conditions; temperature difference reached a maximum of 0.9°C during hours 10-14. Under placebo conditions, body heat decreased steadily throughout the experiment, while oxygen consumption increased. For both drugs, effects were only observed during the first 2 hours.

In condition 4, in which subjects were allowed to move freely, 4 out of 5 subjects remained in the water for 20 hours and the remaining subject for 18 hours. Body heat was paradoxically lower than in the low motor activity condition, but skin temperature was higher. The authors conclude that use of sydnocarb and sydnocarb combined with glutamic acid can improve human thermal status under exposure to cold, thus reliably increasing the maximum time humans can endure extreme cold with relative safety. Effects of the drugs on oxygen consumption may be related to effects on the noradrenergic system and require further investigation.

Table 1: Experimental conditions

Table 2: Criterion parameters of acute chilling in a thermal chamber during control exposure to cold and exposure using drugs

Figure 1: Rectal temperature of subjects swimming for 20 hours

Figure 2: Mean skin temperature of subjects swimming for 20 hours

Figure 3: Skin temperature of the upper surface of the foot of subjects swimming for 20 hours

Figure 4: Heat content and oxygen consumption of subjects swimming for 20 hours

P1039(22/89)* Perkovskiy AV, Adamovich BA, Goncharov IG.
Bacterial protection of outpatients given specialized medical care.
Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.
23(1): 16-22; 1989.
[32 references; 8 in English]

Operational Medicine, Sterile Surgical and Treatment Conditions
Humans, Cosmonauts
Equipment and Instrumentation, Equipment Classification

Abstract: Methods for creating sterile conditions for performance of medical procedures on hospital patients can also be used outside the hospital.(e.g., first aid, or military surgery) and are thus of interest in space medicine. As crews increase in number and space flights grow longer, the likelihood of diseases, such as appendicitis, that require immediate medical intervention increases. Therefore, the spacecraft must be equipped to provide surgical treatment. The authors provide a classification scheme for existing devices and means whereby sterile conditions can be maintained for surgical, contagious, and infection-prone patients. The dimensions considered are: portable vs. stationary/fixed; whole body vs. local; rigid, flexible, or airflow-based. No attempt is made to discuss the existing devices specifically in terms of space flight needs.

Figure 1. Biological isolator

Figure 2: Surgical chamber

Figure 3: Ward with streamlined air flow

PERCEPTION

PAPER:

P1022(22/89)* Tarasenko GI, Shcherbachenko GYe, Petlenko IA.
Synthesized speech -- characteristics of perception under complex acoustic conditions.
Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.
23(1): 35-41; 1989.
[8 references; 4 in English]

Perception, Speech Perception, Accuracy
Humans,
Equipment and Instrumentation, Speech Synthesis, Noise

Abstract: Soviet plans call for the use of speech synthesizers on aviation and space flights to provide more extensive information to crewmembers so as to increase their efficiency and prevent errors during the most critical stages of flight. Acoustic noise is one of the factors which will interfere with accurate perception of synthesized speech signals. Of the speech synthesis methods that do not impose limits on vocabulary, the speech signal can be represented either as a wave form or parametrically. Of the wave representations, "impulse coding modulation" (most likely, what is called in the West "time-domain analysis") is the most common. This method allows representation of natural speech in a digital form. In the time domain methods, signals can be "quantized" at various frequencies, which affects the accuracy of the representation. The most common parametric method is called linear predictive coding and may be based on formant or phonetic analysis. These methods allow use of compressed (clipped) speech.

The study described used a time-domain system with various frequencies of quantization for coding the speech signal and a linear predictive system system using phonetic and all-pole analysis. During the first phase of the experiment a trained (human) reader was recorded [apparently reading some type of meaningful coherent text] on a tape recorder. The same verbal material was generated by the two types of synthesizers. The speech materials were heard by a group of listeners in silence and with noise of 90 and 100 dB intensity. Apparently, the subjects were asked to reproduce what they heard in some way. The time-domain speech synthesizer generated speech with quantization frequency of 8, 12, and 18 kHz. During the second stage of the experiment, a set of nonsense syllables was recorded by a trained reader. Next this material was translated by a linear predictive system and listened to by a group of trained listeners in silence and in the presence of low frequency noise with intensity of 100 dB. Again subjects had to identify what they heard in some way. Phonetic analysis of the response to each syllable was performed under the various conditions to assess intelligibility.

Results (first phase) showed that intelligibility of synthesized speech is highly susceptible to noise interference, in comparison with natural speech. When the quantization frequency of time-domain synthesized speech was highest (18 kHz) its intelligibility improved by 40%. This technique was concluded to be the most promising form of speech synthesis. When speech to be understood involved sets of nonsense syllables, it was found that the phonetic nature of speech perception errors was similar for natural and synthesized (time-domain 18 kHz) speech. The most distortions occurred with consonant sounds n, t, s, f, ts, and m. Although in silence syllables were perceived better in natural speech, in the presence of noise (100 dB) there were fewer distortions of the synthesized syllables. The most common distortions of syllables were not necessarily the same in noise and silence. The differences in results of perception of natural and synthesized speech when coherent speech and nonsense syllables are

used indicated that the process of speech perception involves other factors than those incorporated in existing speech synthesis systems.

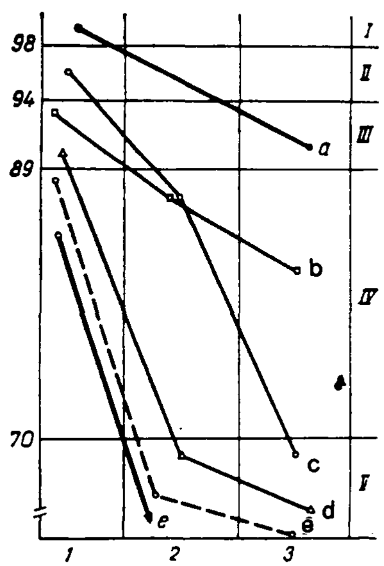
Table 1: Perception matrix of normal speech in silence

Table 2: Perception matrix of normal speech in presence of noise of 100 dB.

Table 3: Perception matrix of speech signals synthesized using time domain analysis with maximal frequency of quantization in silence

Table 4: Perception matrix of speech signals synthesized using time domain method with maximal frequency of quantization in presence of noise of 100 dB

Table 5: Nature of perceptual errors of speech synthesized by the method of time domain analysis (quantization frequency 18 kHz)



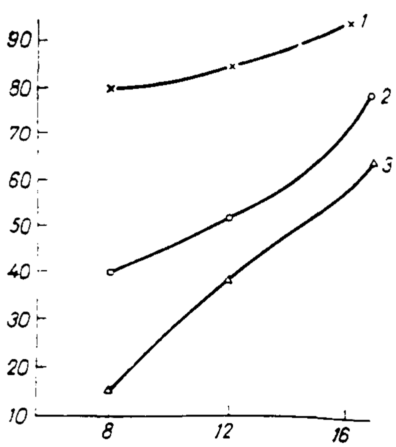


Figure 1: Intelligibility of speech synthesized by different methods
Abscissa: listening conditions; ordinate: verbal intelligibility (in %), a - natural speech; b - all-pole?? synthesis; c - time-domain- 18 kHz; d - clipped speech; e - time domain - 12 kHz; f - time domain - 8 Hz. I - V - intelligibility classes; 1, 2, 3 - silence, noise of 90 and 100 dB, respectively

Figure 2: Intelligibility of synthesized speech as a function of the frequency of its quantization under various acoustic conditions

PSYCHOLOGY

PAPERS:

P987(22/89)* Myasnik Vl.
From Vostok to Mir: Psychological Aspects.
Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.
22(6): 17-23; 1988.
(No references.)

Psychology, Space Psychology
Humans, Cosmonauts
Space Flight, Historical Review

Abstract: This paper summarizes the history of "space psychology" from the flight of Yuryy Gagarin to the current Mir flights. Overall, space psychology has evolved from establishing that man can live and work in space to demonstrating that long-term exposure to the physiological stresses, isolation, and danger of space flight do not necessarily entail serious psychological consequences.

Selection of candidates to be cosmonauts is a major area of space psychology. Original psychological selection procedures were based on the work of F.D. Grobov, particularly his concept of psychological stability. According to the author, Grobov's theories permitted psychologists to:

- evaluate the neuropsychological stability of cosmonaut candidates and select those whose reliability could be strongly predicted;
- identify a set of unusual psychological states, externally similar to forms of behavior, bordering on the normal and amenable to study in a psychological evaluation;
- show that the microgravity leads not only to postural and muscular stress, but to psychological stress as well

During the period 1965-1972, these principles were used to develop a special system of psychological selection of cosmonauts. Selection of crewmembers for Soyuz flights had to consider a number of differences from previous missions. These included: longer exposure to extreme conditions, bigger crews, including more diverse members (not limited to military pilots); the possibility of intragroup situations arising for which accurate prediction of intragroup behavior was difficult. The selection system was developed in the Institute of Biomedical Problems (Myasnikov, Novikov, Kozerenko, Uskov) and in the Central Military Research Hospital (Ioselian). The system utilized the following criteria for expert evaluation: psychological reliability; signs of diminished endurance of "complex living conditions;" and presence of negative personality traits. The system developed is considered by the author to be very effective, particularly for "civilian" crewmembers without previous training for working under stress. While the selection process during the Vostok and Soyuz era concentrated on selection of cosmonauts showing neuropsychological stability and ability to work in spite of functional disturbances, cosmonaut selection for long-term flight was more complex and focused on evaluation of the professionally relevant traits of the candidate as an individual and a social being, as a component of the biosphere, as a biological entity with an inherent genetic program, as the object of monitoring, control and communication while functioning within a man-machine system.

A systems approach was also taken to engendering psychological readiness— defined as a state in which the cosmonaut is confident in his own psychological reliability, aware of the potential resources at his disposal, and able to rationally utilize these resources throughout a long-duration space flight. Such readiness is developed through work on training simulators,

survival training in various climatic and geophysical conditions, aircraft flights, and parachute jumps. The training program involved stress tolerance, active self-regulation of the somatic psychological and autonomic functions, performance when faced with uncertainty and stress, spatial orientation skills, group interactions, endurance, and agility.

Under the direction of Gorbov and Novikov, research on intragroup interactions was performed and the principles, methods, and means for group selection and intragroup management were developed. In this research, the group is viewed as a collective (working group) in which external, socially useful goals prevail over personal and intragroup goals. Based on this approach a principle of "psychological compatibility" was operationalized and has been applied successfully to sports teams and working groups, in addition to cosmonaut crew selection.

Another aspect of space psychology is the expert evaluation of cosmonaut psychological state and work capacity in flight. Today this is achieved through functional diagnosis based on a synthesis of clinical and psychophysiological assessments. Data for these assessments are obtained nonivasively with biotelemetry, and also by using radio and television communications. Using radio and video cameras for psychological diagnosis is based on recent achievements in applied psycholinguistics, development of techniques for spectral analysis of speech, and analysis of behavior based on so-called "communicative movements" (body language), facial expression, gestures, posture, etc. Analysis of these parameters as rated by independent experts with respect to a standardized taxonomy of "asthenic states," fatigue, and work capacity, has led to identification of the most typical maladaptive psychological responses in space (spatial and temporal disorientation; fatigue and asthenization; and transient accentuation of character traits) and allowed their dynamics to be charted throughout the course of a flight.

The data obtained from the above work emphasized the need for a unified approach to studying the efficiency and stress of cosmonaut performance, and the evaluation of their psychological state and work capacity. Work toward this goal was performed between 1980 and 1987. For example, Ryzhov developed a method for quantitatively evaluating the psychological stress on an operator by summing the squared deviations between current and baseline local parameters (EEG, EMG, GSR, HR, RR). Ryzhov and Sal'nitskiy developed a method for evaluating operator performance through analyzing entropy of the hardware system he/she is controlling. These assessments are implemented by computer. Other methods for psychological diagnosis through analyzing man-machine interactions were also developed.

Onboard equipment were developed for the Interkosmos flight of 1971-1978 to experiment on higher psychological functions and operator performance in flight. Automated systems for processing data generated by this apparatus were also developed. The author states that the current state of the art for automated systems in psychological research uses information processing and computational technology and should facilitate the further improvement of space psychology.

Since 1977 the Soviets have had a "psychological support" program to counteract the effects of the impoverished perceptual, informational, social and emotional environments of long-term space flight. Such an approach was first used on Salyut-6. Experience has shown that eliminating the information deficit in space does much to improve cosmonaut mood and performance.

A number of ways for mobilizing psychologically adaptive resources in space have been considered. One method under consideration is the use of oligopeptides, membrane lipids, and catecholamines, which, in appropriate doses, selectively activate and inhibit the autonomic concomitants of negative and positive moods, optimize the phase structure of sleep, and stimulate memory, attention, and learning.

Another important aspect of space psychology is selection of the optimal work-rest schedule. Alyarkinsky leads work on this problem. He was able to prove that there was a discrepancy between the natural rhythm of sleep and wakefulness in cosmonauts when their cycles were compared on Earth and space. This was shown to be due to a phase shift in the sleep-wakefulness rhythm with respect to Moscow time during launch as well as phase migration throughout the course of the flight. This phase shift disrupted circadian rhythm and was correlated with decreased work capacity and increased fatigue. Alyakrinskiy performed a series of experiments which, starting with Salyut-6, made it possible to base the schedule on the spacecraft on Moscow time. He also established the optimal duration of a work session, the optimal number of work shifts per week, the optimal duration of a sleep period, etc. Further research however, showed that more flexibility was needed and different schedules were prescribed for different stages of the flight. Additional work was done on the possibility of adapting to days" varying in length; a correlative principle was developed that selected personnel for critical professions based on their biorhythms.

Another field of space psychology involves psychological engineering. Of particular interest is work to design a manual control system (for example, in rendezvous and docking); develop criteria to evaluate individual safety devices (space suits, antigravity suits); and design information displays. Ground-based trainers and onboard devices with radiotelemetric connections to Earth were used in this research. Starting in 1970, a significant amount of research was done to evaluate the significance of acceleration on perception and processing of information. Results have been used both in training and in device development. Planning of cosmonaut workstations utilized ergonomic ideas.

The author concludes that the accomplishments of space psychology have been notable but a great deal more work needs to be done.

RADIOBIOLOGY

PAPERS:

P990(22/89)*Kovalev YeYe, Ryzhov NI, Sakovich VA.
The problem of radiation safety of space flights in the Interkosmos program.
Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.
22(6): 36-41; 1988.
(19 references; 1 in English)

Radiobiology, Radiation Safety
Theoretical Article, Cosmonauts
Space Flight, Interkosmos

Abstract: In 1964 the Soviets published information they considered essential for ensuring the radiation safety of ongoing and planned space flights. The following were acknowledged to be the major sources of radiation danger in space flight: galactic cosmic rays; protons from solar flares; protons from the inner radiation belt of the Earth; electrons from the outer radiation belt of the Earth; and radiation from nuclear reactors (projected to be a power source on future flights). It was considered desirable from the standpoint of radiation safety to divide flights into low Earth orbit, short-term flights in the Earth's radiation belt, flights in geostationary orbit, interplanetary flights, and flights powered by nuclear reactors.

Low Earth orbit flights are the safest, although they involve exposure to protons from the Earth's radiation belt and there is some risk of exposure to protons from solar flares passing through the magnetosphere. It is now known that the mean yearly radiation dose during flight in a modern space station is about 5-10 rem, even under calm radiation conditions. From the beginning it was recognized that the most difficulty was presented by long-term interplanetary flights, which at that time were expected to begin relatively soon. The yearly dose of galactic radiation alone was estimated for maximal solar activity to be 50 rem and during minimal activity 100 rem.

In the mid 1960s the Soviets formulated the major scientific goals with respect to radiation safety during space flight. The most difficult aspect was finding a basis for standards: standards used on Earth were considered too stringent, considering the cost of shielding in space and the exemplary health of cosmonauts. These differences made it necessary to study the radiobiological effects of cosmic radiation. The task was made more difficult by the stochastic nature of solar proton events. A second task involved considering how temporal and spatial inhomogeneity of radiation exposure affected radiobiology. The pattern of cosmic radiation doses to tissues was studied and the efficacy of pharmacological countermeasures against cosmic radiation was determined. Further study of the physical nature of cosmic radiation was also required. These problems were addressed using proton beams with energy of 660 MeV accelerated by a synchrocyclotron, cyclotron, and synchrophasotron.

Cooperation among Communist countries in the areas of space radiobiology and dosimetry began in 1967 with the formation of the space biology and medicine working group within the Interkosmos program. At this point, initial results on the accelerator of the Laboratory of Nuclear Problems in Dubne had already been obtained. In experiments on a variety of laboratory animals, plant cells, bacteria, and algae, it was determined that the relative biological effectiveness of protons in the energy range of 50-660 MeV supported use of the quality factor-linear energy flow function in the range of LEF up to 1500 MeV/cm^2/g to compute equivalent dose. In larger animals, the interaction of protons with tissue substance also had to be considered. In 1967 criteria for radiation safety were set for flights up to 1 month in duration. The acceptable dose was 15 rem, at which no appreciable immediate somatic effects occurred. The justified risk dose was 50 rem, at which mild symptoms of primary

radiation reaction occurred only in rare cases. The critical dose was established at 125 rem, at which a decision had to be made whether to continue a flight. It was recommended that during a solar proton event, a crew in low Earth orbit retreat to the recovery vehicle where shielding is thickest.

The next stage of radiation safety research was associated with preparations for interplanetary flight. This involved research using accelerated multicharged ions on the ground, actual space flight research, and chronic irradiation with γ sources. This stage marked the beginning of actual collaborative research within Interkosmos. Relative biological effectiveness of multicharged ions with energy of 300-5000 MeV accelerated on a cyclotron had to be studied at the cellular level, due to short path length. Soviet-East German experiments with cells of *E. coli* bacteria, *in vitro* cell cultures, *chlorella*, seeds and corneas of mice enabled formulation of mathematical models describing the bioeffects (RBE) of these particles. It was determined that for values of LET greater than 2000 MeV cm^2/g, the value of the quality factor of ionizing radiation may be elevated for cosmic rays.

At the end of the 1970s, the USSR conducted joint studies with Bulgaria to investigate beams of α particles and carbon and nitrogen ions accelerated on a synchrophasotron up to energy of 4.5 geV/nuclon. Because of the longer path length of these particles, effects were studied at the level of the whole organism as well as on the cellular level; emphasis was placed on effects on brain cells. As is the case with galactic radiation, secondary radiation arising due to interactions in the tissues is important. Results confirmed the need to make regulated values of quality factors more exact for space flight radiation standards.

A third line of Interkosmos research involved chronic gamma irradiation of 246 dogs. Over the course of 3 and 6 years, subjects were irradiated at mean annual doses of 21, 62 and 125 rad. Only with a dose as high as 360-380 rad were effects such as biochemical changes in tissues, decreased functional capacity of the cardiovascular system, and disruption of thermal regulation observed. Czech radiobiologists performed parallel studies on the chronic irradiation of small laboratory animals. All these studies led in 1975 to the publication of "Temporary standards of radiation safety for space flights." Unlike standards for exposure on Earth, this document stipulated no maximum acceptable dose, but instead set standard levels of radiation, which are a nonlinear function of flight duration, and cited the probability of these doses being compounded by solar proton events, which must not exceed 1%. This was the first practical use of stochastic criteria for radiation safety. The standard level for space flight over a year was established as 150 rem, substantially higher than the maximum acceptable doses set for Earth.

Space flight studies supplement results obtained on Earth. On COSMOS-690, studies were conducted of the combined effects on vital physiological systems of radiation (from an onboard γ-ray source) and other space flight factors. Czech scientists also participated in these studies. Chromosome aberrations were studied in seeds hit by heavy ions of galactic radiation on COSMOS-782, -936, -1129, and -1514.

A significant milestone in dosimetry was the Soviet-Bulgarian development of a phantom-manikin of the human body made from tissue equivalent plastic. Radiobiological experiments used thermoluminescent dosimeters developed in Hungary. A system that comprised these dosimeters and a portable instrument panel is routinely used on space stations for individual dosimetry and measurement of radiation conditions in the station compartments, as well as for flight experiments. Plastic track detectors were developed jointly with specialists from Hungary, East Germany, Romania, and Czechoslovakia for use in radiobiological experiments.

Recent experiments have measured the level of cosmic radiation in thin surface layers, a matter of some importance with regard to EVAs. In 1975, the East Germans developed a mathematical model explaining the relationship between RBE and LET. This model was adapted in the USSR specifically for consideration of the effect of dose rate on cell viability.

P1037(22/89)* Davydov BI, Tikhonchuk VS, Zuyev VS.
Epidemiological observations (follow-up) of exposure to microwaves (neurophysiology, hematological, and ophthalmological effects).
Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.
23(1): 4-11; 1989.
[35 references; 21 in English]

Biological Effects; Neurophysiology; Hematology; Opthalmology
Review Article; Humans
Radiobiology; Microwaves

Abstract: The authors review neurophysiological, hematological and opthalmological effects of exposure to microwaves. In neurophysiology, it has been found that after acute (short-term) exposure, the response in animals is similar to documented thermal effects Convulsions have occurred at high, nearly fatal doses, but responses at low doses (< 1 W/kg) are more variable. U.S. technicians exposed to 3200 times the standard U.S. dose complained of nausea, anxiety, dizziness, poor appetite and hypersensitivity to light, but none of these symptoms persisted. A Soviet study of women who had long-term occupational exposure to microwaves concluded that after 7-14 years adaptive capacities are disrupted, expressed by decreased α- and increased β-rhythms. An Italian study concluded that heightened anxiety and depression occurred in workers after long-term occupational contact with microwaves. French researchers recorded complaints of memory loss. Other field studies of psychological effects have had mixed results. Experimental exposure to microwaves can give rise to auditory sensations.

In hematology, Soviet authors have concluded that chronic exposure to microwave fields with flux density less than 1 mW/cm^2 can give rise to changes in blood constituents, especially leukopenia. However, most authors note that these changes are not statistically reliable even when subjects are irradiated until they experience sensations of heat. Follow-up studies that investigate cause of death in workers occupationally exposed to microwaves have also been negative. *In vitro* studies have revealed no functional or chromosomal impairments in human lymphocytes, even at absorbed doses of 200 W/kg over a period of 20 minutes. Although studies have revealed no effects, the authors argue that given sufficiently high doses (considerably greater than 4 Wt/kg) over long periods of time, hematological effects would be observed. Cataracts have been the best-studied of the effects of microwave exposure. Cataracts have been corrleated to microwaves since 1948, although the mechanism of their induction is still not understood.

Table 1: Death rate from accidents and diseases of radar and radio equipment operators and technicians

Table 2: Some clinical manifestations of eye damage due to exposure to radio and microwaves

REPRODUCTIVE SYSTEM

PAPER:

P983(22/89)* Denisova LA, Tikhonova GP, Ananasenko ZI, Pustyynnikova AM, Ivanov YuV, Kolomiyets OL, Mazurova TF.
Study of the reproductive function of male rats after space flight on COSMOS-1667 biosatellite.:
Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.
22(6): 58-63; 1988.
(13 references; 3 in English)

Reproductive System, Reproductive Function; Developmental Biology, Prenatal and Early Postnatal Development
Rats, Male
Space Flight, COSMOS-1667

Abstract: The goal of this research was to evaluate the reproductive function of male rats exposed to space flight on COSMOS-1667 and the state of their ensuing offspring. Subjects were 10 white rats exposed to 7 days of weightlessness when they were 3 months old. A vivarium control and a synchronous group (housed in a mock-up of the biosatellite and exposed to all physiologically significant space flight factors aside from weightlessness) were used. All three groups were provided with a paste-like food and *ad lib* access to water. Seven animals in the experimental group were sacrificed 6-10 hours after landing. They were dissected and the testes and epididymi were isolated and weighed. Smears were prepared from homogenates of the testes and stained with azure-II-eosin. Reproductive cells were identified and counted, and the maturity stage noted. Cells examined included: spermatogonia, spermatocytes, spermatids, spermatozoids, Sertoli cells, and Leydig cells. The area of the nuclei was measured in Sertoli cells using a projection technique. The spermatozoids in the epididymi were also counted. The number of morphologically anomalous spermatozoids and other atypical elements were counted in smears prepared from a suspension of the epididymus. The dark blue complexes of spermatocytes were examined with an electron microscope. Control groups were treated analogously.

Three males from the experimental group, 3 from the synchronous control, and 6 from the vivarium group were placed in cages with normal females in a ratio of 5 females to 1 male to study sexual activity and resulting offspring. Breeding began 1 day after reentry; the males were given access to the females for 15 days. During this period the ejaculate of the flight animals consisted of gametes which had been exposed to space during various stages of spermatogenesis — from the stage of late spermatids to mature gametes. Vaginal smears were taken from the females daily to determine the onset of pregnancy. A coefficient of sexual activity was computed for the males based on length of exposure to the females before mating and the percent of impregnated females. The females were allowed to give birth at their natural term. A number of parameters reflecting the status of the offspring were used to evaluate the genetic worth of the spermatozoids, including: number of live and stillborn neonates in a litter, ratio of males to female, congenital anomalies of the visceral organs and skeleton.

A total of 58, 37, and 40 neonate rats in the experimental, synchronous, and vivarium control groups, respectively, were observed during the postnatal period. Postnatal death rate, overall clinical state, dynamics of weight gain, age at unfolding of the ears, age when eyes opened, dentition development, development of coat, and general activity level on a horizontal surface were studied in the neonates. Physical endurance and vestibular sensitivity of these neonates were estimated on the basis of the time taken to turn over onto the stomach on horizontal and inclined surfaces. On days 7, 12, and 17 after birth, the animals' static endurance was tested by recording the time the râts could hold on to a crossbar. On day 30 of life, characteristics of

orienting and exploratory responses in an "open field" were assessed. Parameters recorded included horizontal and vertical motor activity, visits to the central area of the field, relative path length in this area, duration of grooming, and frequency of excretion. Results were processed using t-tests and analysis of variance techniques.

Growth rate of the male rats during the 7-day flight and the weight of the experimental animals on reentry were virtually identical to those of the vivarium control, as were mean testes weights.. No differences were found in epididymus weights, proportions of major cellular elements nor in the size of Sertoli cell nuclei. Germinative indices were virtually identical. The number of spermatozoids in the epididymus of flight animals was somewhat greater than that in the controls; no significant differences were found in quantity of atypical or degenerate forms of spermatozoids. Electron microscopy suggested that exposure to space for 7 days did not increase frequency of chromosome aberrations. No differences were noted in the sexual activity of the three groups observed. Time after exposure to females before mating and number of impregnated females were also virtually identical. Increased perinatal deaths were not observed in the offspring of flight males,nor were there differences in neonate weights. Increased internal or skeletal anomalies were not observed. None of the early developmental and behavioral parameters differed among the various groups. A decrease in testosterone had been noted in the flight animals immediately after reentry, but because reproductive function was normal this decreased hormonal level was attributed to dynamic reentry factors. It was noted that these results differ from results of a Spacelab-3 experiment in which decreased testes weight and diminished spermatogonia pool were observed in male rats exposed to space for 7 days.

Table: Results of breeding male rats exposed to space on biosatellite COSMOS-1667 with intact females

Grp	# males	# females	% females pregnant	% viable pregnancy	# neonates per female		Weight of 1 neonate, g	% males in litter
					live	stillborn		
F	3	19	68	52	12±1	0.6±0.5	5.7±0.2	50.2±3.3
SC	3	15	87	54	13±1	0.3±0.1	5.4±0.1	42.4±7.5
VC	6	41	73	37	10±1	0.6±0.4	5.8±0.1	47.1±4.8

F = flight group; SC = synchronous control; VC = vivarium control.

Synaptonemal complex of rat spermatocytes at the pachytene stage

a - in the norm (vivarium control). Mag. 15,000; b - breach in the structure of a synaptonemal complex (synchronous group). Mag. 10,000; c -shortening of the end of the lateral element of the synaptonemal complex (synchronous control) Mag. 11,00;0 d - microloop? in the structure of the lateral element of the synaptonemal complex (experimental group) Mag. 16,000.

SPACE BIOLOGY AND MEDICINE

PAPERS:

P991(22/89)* Il'in YeA.
The COSMOS biosatellites: Some conclusions and prospects.
Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.
22(6): 41-50; 1988.
(25 references; 6 in English)

Space Biology and Medicine, Life Support Systems, Adaptation, Body Fluids, Cardiovascular and Respiratory Systems, Endocrinology, Metabolism, Musculoskeletal System, Neurophysiology, Radiobiology
Review Article, Dogs, Primates, Rats
COSMOS Biosatellites, Equipment and Instrumentation, Artificial Gravity

Abstract: The COSMOS series biosatellites have played a leading role in solving problems in space biology during the era of manned space flight. These problems have included identifying the effects of weightlessness on the fundamental vital processes, the mechanisms underlying the structural and functional restructuring that occur in various physiological systems, and the characteristics of the combined effects of weightlessness and cosmic radiation, as well as the effects of artificial gravity. The Institute of Biomedical Problems of the USSR Ministry of Health has played leading role in research design and interpretation, while the "Biofizpribor" design bureau has had the primary responsibility for equipment design.

On the first biosatellite, COSMOS-110, the two dogs serving as subjects were maintained by a life support system by suits in which they were restrained by nylon straps that held them in the right position for waste collection and allowed them to move their legs without changing their positions. They were fed and given water once a day through fistulas created in their stomachs long before the flight.

Automated life support for primate subjects were flown on COSMOS-1514, 1667, and -1887, with two primates participating in each flight. The primate capsule is illustrated in the figure. The monkeys were strapped rather rigidly to the primate chair in the area of the pelvis, where there was an opening for collecting wastes. The animals' upper body and limbs were allowed relatively free movement. Before launch and reentry a special system of straps fixed the animals to their chairs. The two monkeys on each flight were able to see each other through the transparent walls of the capsule.

Rats were flown on COSMOS-605, -690, -782 and -936, using a specially designed system for each individual animal. This system consisted of a cylindrical cage with a feeding and watering apparatus, lighting, and a device for telemetric monitoring of body temperature and motor activity. Cages were ventilated with a constant directed flow of air through an opening in the upper portion. . The cage had a grid floor with a waste collector, and were large enough that the animals could move and shift position. For the COSMOS-1120, -1514, -1667, and 1887 flights, rats were housed in groups of up to 10.

Studies of the effects of artificial gravity used rats and an onboard centrifuge with a radius of 320 mm. There were two such centrifuges on COSMOS-936, rotating at a rate of 53 rev/minute and creating artificial gravity of approximately 1 g. Five rats, housed in individual cages, were rotated on each centrifuge. Continuous exposure to artificial gravity was 18 days. A control group not exposed to artificial gravity was housed on the same flight.

Combined effects of weightlessness and ionizing radiation were studied in rats in individual cages on COSMOS-690. Two groups were irradiated at doses of 220 and 800 rad using a specially designed device with ^{137}Cs as the radiation source.

For all animal experiments the following atmospheric parameters were maintained: O_2 within the range 150-210 mm Hg; CO_2 up to 10 mm Hg, relative humidity 30-70%; temperature 21-25°C, barometric pressure 715-780 mm Hg, with harmful contaminants maintained within acceptable levels.

To prepare them for flight, animals first underwent clinical selection, training, and exposure to isolation and limited motor activity; conditioned responses were developed, electrodes were surgically implanted, and baseline data were recorded.

Due to technical limitations, a relatively small number of parameters were recorded for rats in flight: motor activity and body temperature. On COSMOS-110, polygraphic recordings were made of the cardiovascular parameters of the dogs. A total of 12 parameters were recorded from the monkeys to provided information on the state of the central nervous, vestibular, cardiovascular, motor, and thermal regulation systems.

Most of the data were obtained after the rats were sacrificed postflight and morphological and biochemical analyses performed. For dogs and monkeys, postflight studies were continuations of inflight ones. Postflight studies were begun at the reentry site in specially developed field laboratories, equipped for a variety of investigations at any time of year. Subsequent studies of animals and biopsy material were conducted in scientific laboratories in the USSR and abroad.

The experiments on the record 22-day flight of COSMOS-110 in 1966 were concerned mainly with the cardiovascular system. Unfortunately, some of the experimental apparatus broke down in flight and experimental goals could not be fully realized. Despite this failure, a number of important results were obtained including: 1) heart rate dropped during flight; 2) duration of contraction and ejection period reflected the myocardial hypodynamia syndrome; 3) circulating blood volume decreased, as did blood filling of the heart. Postflight studies using provocative tests confirmed that cardiovascular deconditioning developed in flight. During the postflight period there were striking disruption of motor skills, similar to those occurring after cerebellum damage: ataxia without evident disruption of muscle sensation, dysmetria, synergy of movements of fore and hind limbs, and some adiadochokinesis. Body weight loss was 26 - 29% of baseline, with large decreases in fluid, muscle mass, bone mineralization, and calcium balance. Blood studies revealed decreased total protein, relative concentration of albumin fractions, and plasma volume. There were also signs of inflammatory processes, especially in the stomach fistula. Results were confounded somewhat by the negative effects of the rigid fixation system used throughout the flight and other methodological defects.

A total of 6 monkeys (rhesus macaques) have been used on three biosatellite flights; the primary goal of these experiments was to investigate physiological responses to weightlessness during the initial (days 5-7) and transitional (day 13) stages of adaptation to weightlessness. The monkeys' responses were highly subject to individual differences. During the first 1-2 days all subjects were drowsy and moved little. Subsequently, normalization progressed at different rates. Some monkeys displayed edema of the face and neck during the initial 2 days, which had not disappeared completely after 7 days. Certain monkeys showed slowed heart rate and gradual decrease in body temperature with altered thermal biological rhythms. Others showed virtually no changes in these parameters. Due to equipment failure, one monkey ceased to receive solid food starting on day 2 of flight and this intensified differences in responses. This same monkey freed itself from some restraints, making certain studies impossible. Vestibular functions were investigated with two provocative tests, one involved bringing the animals to vertical posture in the primate chair and the other moving the head in the direction of a light signal. Recorded neuronal electrical activity during flight in response to vestibular stimulation showed greater excitability of both the otolith and semicircular canals, with the latter occurring earlier in flight. By days 5-6, these responses had normalized. Changes were also noted in regulation of eye and head movements, which did not fully normalize during flight. No marked adverse effects were found in conditioned instrumental reflexes. Changes were seen in several of the monkeys in linear blood flow in the carotid artery. No substantial changes were observed in blood pressure or EKG recordings.

Several changes were noted in motor function. Amplitude of electrical activity in hindlimb muscles decreased. Starting on day 2, decreased motor effort was compensated for by recruitment of additional motor units. On day 5, there were signs of disrupted central mechanisms for regulating motor activity. Normalization did not occur during the 5-7 day flights. When the monkeys were examined at the reentry site, all were judged to be in good shape. They were active and responded appropriately to the experimenters. COSMOS-1887 landed at an unscheduled site delaying the first examination for 20 hours after reentry. After the 13-day flight, one monkey was active and reacted appropriately to the environment; the other,, which had received no solid food for 11 days, was lethargic and pale and did not react to examining personnel. This monkey responded well to subsequent treatment, including a special strength-building diet.

The state of rats during flight on COSMOS biosatellites in flight was fully satisfactory, judging by their good appetites and retention of normal diurnal rhythms in motor activity and body temperature. Postflight dissection revealed no pathological changes, but some structural and functional changes indicated adaptation to weightlessness. No changes were observed, however that could not also be attributed to exposure to other environmental factors. Endocrine and lymphoid responses were characteristic of moderate chronic stress response. Musculoskeletal changes were similar to responses to dynamic and static unloading and included decreased mass and cross-sections of muscle fibers, partial transformation of slow twitch fibers into fast-twitch ones, decreased volume of sarcoplasmic nets, and decreased strength. Severity of changes was a direct function of the involvement of the muscles in maintaining posture on Earth. This was also the case for bone, where changes included retarded osteogenesis, osteoporosis, demineralization, and decreased density and mechanical strength. Other studies implicated the kidneys in the changes observed in fluid electrolyte metabolism during space flight. Structural changes in the otolith membrane were noted, evidently associated with disruption of calcium metabolism and formation and outflow of endo- and perilymphs ions the vestibular system. COSMOS experiments demonstrated that even 7-day flights lead to structural, metabolic, and functional shifts, which which become more pronounced with longer flights. Rat data were used to anticipate cosmonaut responses to long-term flight and design countermeasures.

Centrifugation studies on COSMOS-936 indicated that artificial gravity is a promising means of maintaining optimal physiological status on long-term flights. Use of artificial gravity at a level of 1-g prevented structural and functional changes in the circulatory, endocrine, musculoskeletal, and other systems. Irradiation studies showed that weightlessness does not substantially modify the adverse effects of radiation. These data were used to develop radiation safety standards for flights up to 1 year in duration.

Ontogenetic studies on COSMOS-1514 indicated that despite substantial changes in pregnant females exposed to space, offspring were essentially normal.

For the future, 14-day flights are planned for two biosatellites, one in 1989 and one in 1991. Planned experiments include:

Monkeys (both satellites):

- vestibular and higher nervous system function: study of adaptation of mechanisms responsible for spatial orientation, eye movements, and motor control to altered activity of vestibular structures in weightlessness; study of the vestibulomotor reflex interaction under conditions of sensory deprivation;

- cardiovascular research: study of the regulatory mechanisms of central and peripheral (organ) hemodynamics at various stages of adaptation to weightlessness;

- bone research (postflight): study of the possibility of predicting the sensitivity of various components of the skeleton to lack of gravitational loading; study of the mechanism linking skeletal strength and bone demineralization;

- thermal homeostasis research: study of thermal comfort, regional heat emission and its regulation in weightlessness;

- metabolic research: study of mineral, protein, fat, carbohydrate and other types of metabolism.

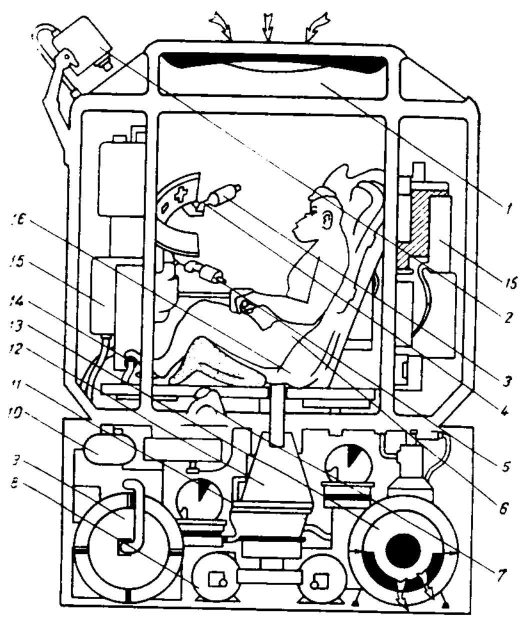
Monkeys will have transmitters implanted in various parts of the brain, and for measurement of arterial, venous, and intracranial blood pressure. The number of instrumental conditioned reflexes the animals will perform in flight will be increased. EMG measurement units will be implanted in muscles of various types.

Rat experiments will utilize loading tests; post-traumatic regeneration of tissues will be studied, and a number of new research methodologies employed. Whenever possible apparatus flown on COSMOS-1887 will be used on the 1989 satellite, with appropriate improvements and modifications. Apparatus for gathering and preliminary processing of physiological information from the monkeys will be new. A thermal comfort device developed by the Czechs will be used in the capsules housing the monkeys.

A new generation of apparatus will be developed for the 1991 flight. It is anticipated that the monkeys will be allowed greater freedom of movement for their arms. Separate collection of liquid and solid wastes will make metabolic studies possible. Containers for housing rats will be enlarged to accommodate up to 12 animals (in two groups of 6). Work has started to develop habitats for studies of fruit flies, beetles, and other subjects.

Table: Biological research on COSMOS biosatellites

Mission	Launch Date	Flight duration, days	Biological subjects
COSMOS-110	2/22/66	22	Dogs (Ugolek and Veterok), plants, seeds, bacteria, and others
COSMOS-605	10/31/73	22.5	45 rats, tortoises, bacteria, lower plants, flour beetles, and others
COSMOS-690	10/22/74	20.5	35 rats, higher plants, lower plants, bacterial cells, tortoises, etc.
COSMOS-782	11/25/75	21	25 rats, fish, fish roe, animal and plant tissue cultures, yeast, fruit flies ,and others
COSMOS-936	8/3/77	18.5	30 rats, higher and lower plants, fruit flies and others
COSMOS-1129	9/25/79	18.5	37 rats, insects, higher and lower plants, animal and plant tissue cultures, lower fungi, bird eggs, and others
COSMOS-1514	12/14/83	5	Monkeys (Abrek and Bion), 10 rats, fish, plants, and others
COSMOS-1667	7/10/85	6.5	Monkeys (Vernyy and Gordyy), 10 rats, fish, fruit flies, tritons, higher plants, plant seeds, and others
COSMOS-1887	9/29/87	13	Monkeys (Drema and Yerosha), 10 rats, unicellular organisms, spores, plant tissue cultures, seeds and sprouts of higher plants, insects, fish, tritons and others



Capsule for maintaining monkeys in flight

1- lamp; 2 - television camera; 3 - nozzle for delivering juice; 4 - light indicator panel; 5 - nozzle for delivering food; 7 - device for vertical displacement of chair; 8 - ventilator; 9 - food container; 10 - juice container; 11 - filter for removing harmful contaminants from air; 12 - waste collector; 13 - filter for bacterial cleaning of the air; 14 - lever of leg actograph; 15 - scientific apparatus; 16 - chair base.

P986(22/89) Grigor'yev AI, Yegorov AD.
Phenomenology and mechanisms underlying changes in the major functions of the human body in weightlessness.
Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.
22(6): 4-17; 1988.
No references.

Space Biology and Medicine, Adaptation, Body Fluids, Cardiovascular and Respiratory Systems, Endocrinology, Hematology, Immunology, Metabolism, Musculoskeletal System, Neurophysiology
Humans, Cosmonauts, Review/Theoretical Article
Space Flight

Abstract: This ambitious article summarizes and describes the mechanisms of the major changes observed in humans in response to exposure to weightlessness. An overview of these changes is given as follows:

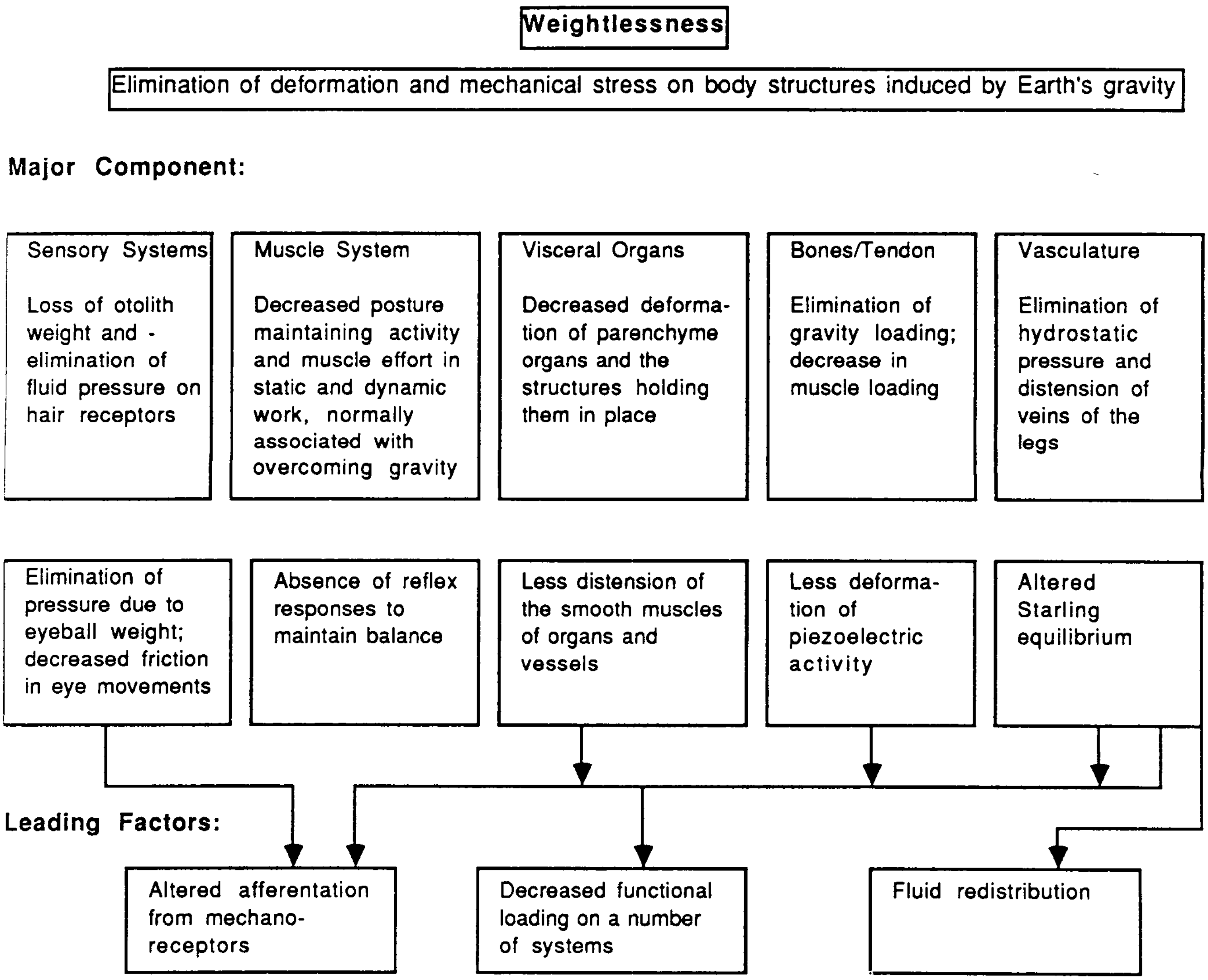
1. Initial phase of flight (week 1):
   - Symptoms related to the redistribution of body fluids;
   - Space motion sickness;
   - Changes in the general nature of motor activity and coordination of motor acts.

2. Long-term exposure to space:
   - Changes in hormonal status;
   - Changes in motor system and muscles;
   - Changes in fluid-electrolyte metabolism and the corresponding regulation system;
   - Changes in hemodynamics with the development of cardiovascular deconditioning;
   - Changes in calcium metabolism and mineralization of bone tissue;
   - Functional erythropenia;
   - Decrease in immunological reactivity

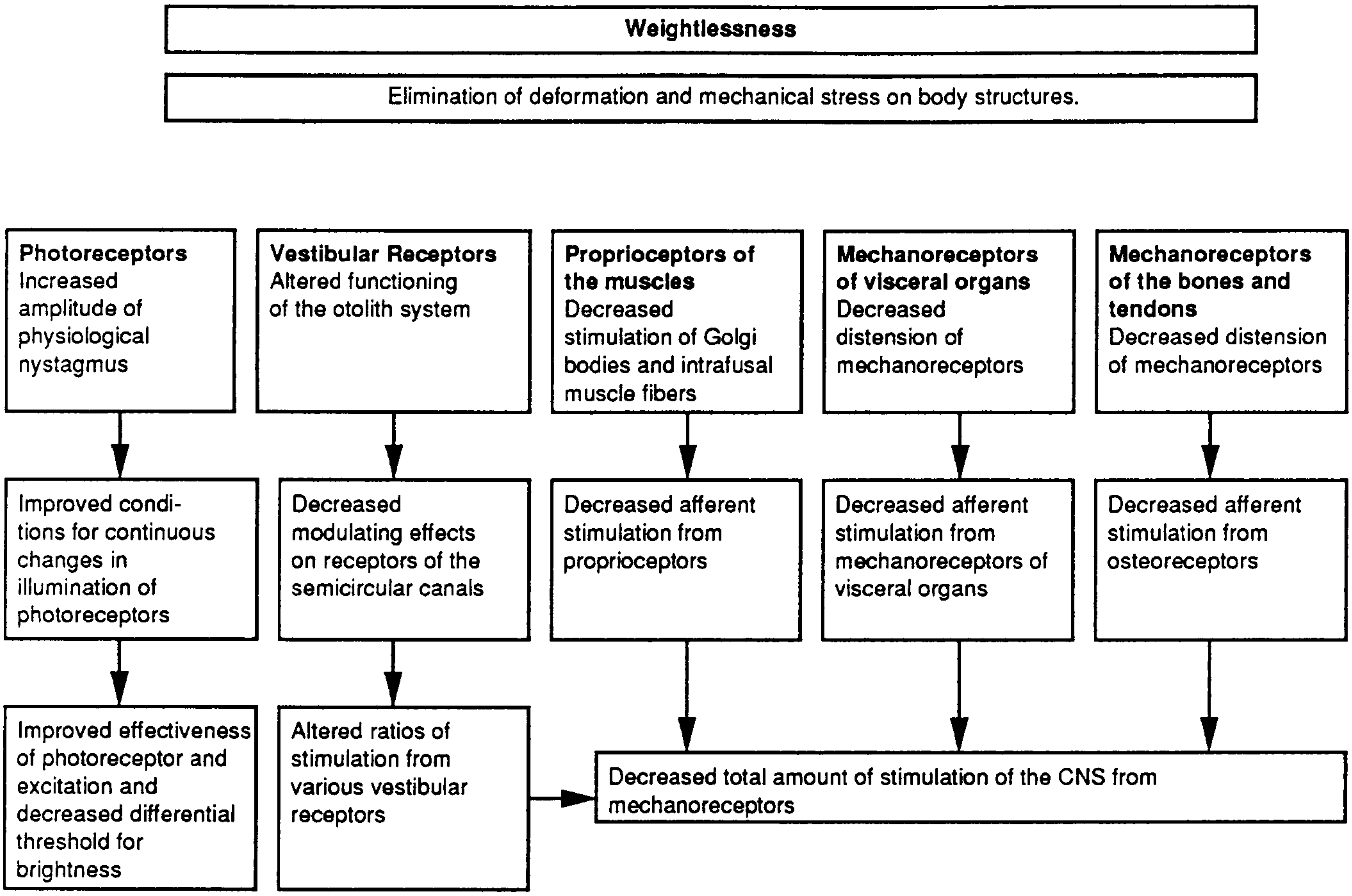
Existing knowledge of these changes occurring is best summarized by the following diagrams

SPACE BIOLOGY AND MEDICINE

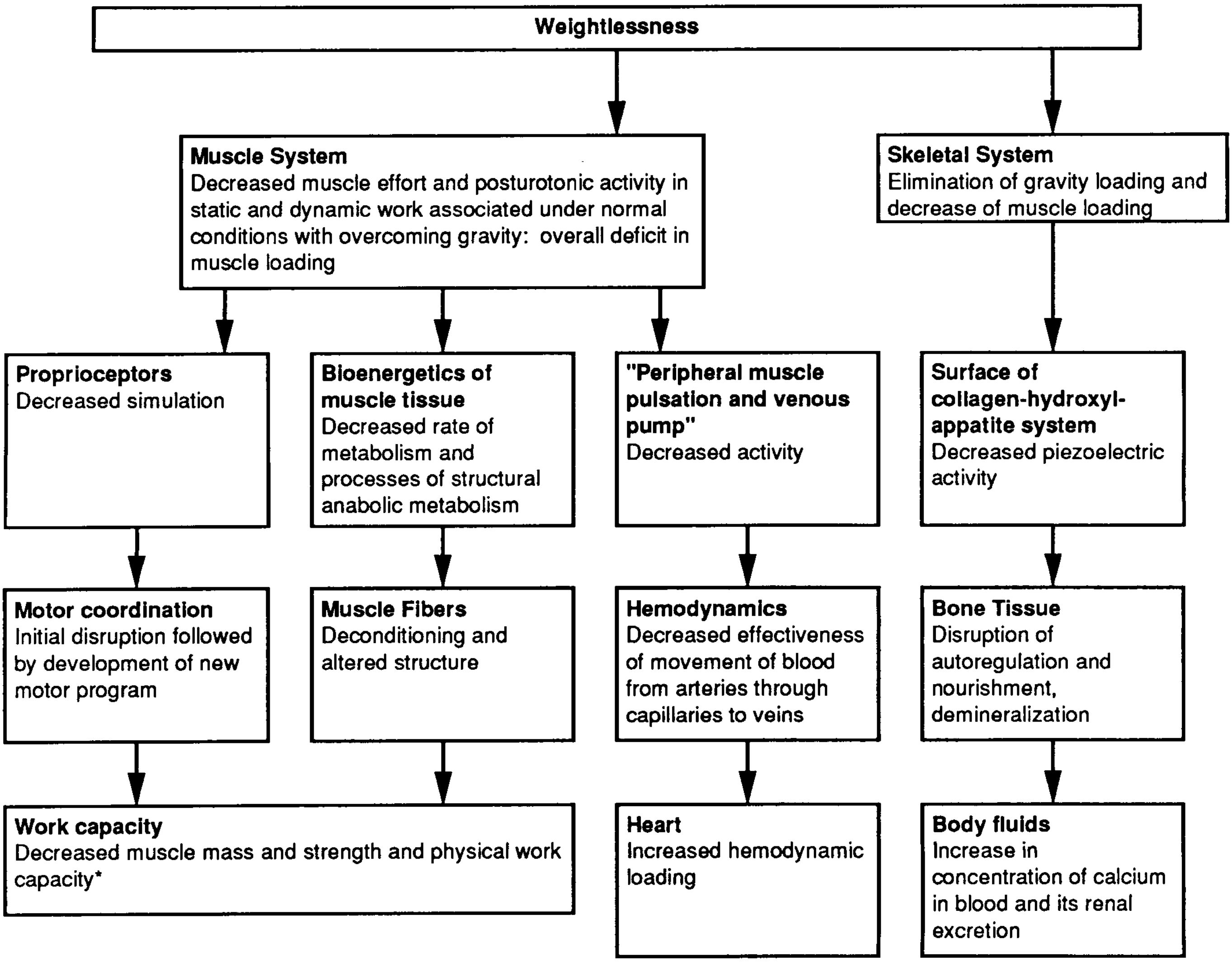
1. Physical effects of weightlessness on the major physiological systems.



2. Changes in afferent stimulation in weightlessness.



3. Effects of weightlessness on the musculoskeletal system



*Data obtained on space flights

4. Physiological reactions to elimination of hydrostatic pressure of body fluids under conditions of weightlessness

Weightlessness
Elimination of hydrostatic pressure in body fluids

Initial reactions
(hours, days)
Changes in deformation of vasculature and Starling equilibrium that differ in direction for areas above and below the level of the heart

Indirect effects of fluid shifts I the cranial direction
Increased blood volume and pressure in the cardiopulmonary region, initial increase in stroke volume* and cardiac minute volume*, and in blood flow and pressure in renal vasculature

Rapid adaptive reactions
(hours, days)

Kidneys
Initial inhibition of activity of renin-agiotensin -aldosterone system increased diuresis and electrolyte excretion

Cariopulmonary region
Narrowing of pulmonary vessels, expansion of systemic circulation vessels* and pooling of blood in visceral organs; reflexive inhibition of ADH hormone*

Blood
Decreases in plasma volume,* circulating blood volume and interstitial fluid, relative increase in erythrocyte mass and hemoglobin concentration

Delayed adaptive reactions
(days, weeks)

Kidneys
Increased level of angiotensin in blood plasma*; Increased production of natriuretic factor and prostaglandins; Increased excretion of aldosterone,* sodium,* potassium*

Blood
Inhibition of erythropoiesis*; Decreased total volume, erythrocyte mass* and hemoglobin concentration; Further decrease in circulating blood volume.

Circulation
Establishment of a balanced flow of blood to heart; Decreased stroke* and heart volume; Tendency of phase structure of cardiac cycle to normalize*

Completion of development of adaptive reactions and redistribution of blood with partial normalization of initial shifts

Establishment of a new level of functioning of the circulatory system and fluid-electrolyte balance with decreased plasma volume, altered reactions to stress, and decreased gravitational tolerance

*Data obtained on space flights

5. Mechanisms underlying development of a new level of functioning under conditions of weightlessness

Weightlessness

Elimination of deformation and mechanical stress on body structures normally due to Earth's gravity, absence of hydrostatic pressures

Mechanoreceptors in CNS
Decreased total amount of afferent stimulation; decreased activity of the dorsal (sympathetic) portion of the hypothalamus; predominance of vagal tonus

Fluid shifts
Increased central blood volume, pressure and occurrence of reflex response from the mechanoreceptors for low pressure; initial increased venous return,, stroke volume,* cardiac minute volume,* and decreased pressure gradient*

Musculoskeletal System
Overall deficit in muscle loading; development of deconditioning of the muscle system* decrease in activity of peripheral muscle pulsation and in effectiveness of venous pumps

↓

Systemic and pulmonary circulation
Decreased tonus and pressor reactions of small vessels, narrowing of pulmonary vessels, widening of systemic vessels,* decreased peripheral resistance,* pooling of blood in visceral organs

Fluid-electrolyte metabolism
Reflexive inhibition of AHD excretion*
Increased excretion of fluid and electrolytes*
Altered ratios of electrolytes in body fluids*

Cardiac activity
Initial increase in volume, followed by hydraulic resistance, increased systolic work and sucking function of the heart in moving blood, intensified cardiac activity, restructuring of the phase structure of the cardiac cycle*

↓

Completion of the rapid adaptive reactions
Decreases in plasma volume,* circulating blood volume,* and interstitial fluid,* relative increase in erythrocyte volume and mass* and hemoglobin concentration*, further decrease in circulating blood volume*

↓

Blood
Inhibition of erythropoiesis, decreases in erythrocyte volume and mass* and hemoglobin concentrations*, further decrease in circulating blood volume*

Circulation
Establishment of balanced flow of flood to the heart, decreased stroke volume, volume of the heart and elastic resistance (decreased blood pressure*), tendency for cardiac cycle phase structure to normalize

↓

Establishment of a new level of functioning for the circulatory system, with decreased tolerance of gravity,* stabilized reaction due to inclusion of reflexes of the carotid sinus

*Data obtained on space flights

The following directions for research on future long-term space flights are suggested:

- detailed study of the phenomenology and mechanisms underlying changes in the major physiological functions and differentiation of specific shifts caused by the physical nature of weightlessness and adaptive responses occasioned by it;

- performance of special investigations directed at studying the physiological systems and "weak spots" which could limit long-term exposure of humans to space;

- development and modernization of principles, methods, and countermeasures to prevent disorders developing in response to space flight factors;

- development of theories, methods and practical implementations of control of the general health and work capacity of space flight crewmembers;

- goal-directed utilization of weightlessness as a means for the study of general biological problems of the effects of gravity on living systems and identification of gravity-dependent and -independent physiological processes.

Special Feature: A Year in Weightlessness

Interview with Soviet cosmonauts V. Titov, and M. Manarov; interviewer: I. Nekhamkin; *Sovetskiy Soyuz,* No 2, 1989.

On 21 December of last year, the Soyuz TM-6 descent module landed in Kazakhstan, not far from Dzhezkazgan. It was bringing cosmonauts Vladimir Titov and Musa Manarov and the French cosmonaut-scientist (payload specialist) Jean-Louis Chretien home from space. The Soviet cosmonauts had lived and worked in orbit for exactly a year, actually a leap year with 366 days. Their French colleague, a member of the second Soviet-French visiting crew, had been in space for 25 days.

Man is continuing to conquer space in the name of science and practical benefits for the entire planet. The Mir cosmonauts completed an extensive program of astrophysical, geophysical, and medical research and technological and biotechnological experiments on board the space station. An important component of the enormous amount of data that was gathered was generated by biomedical observations and studies, in which the cosmonauts themselves served as subjects.

Today the scientific communities of a number of nations are discussing prospects for a flight of an international space crew to Mars, and for this reason the year-long flight experience of V. Titov and M. Manarov is truly invaluable. It provides a basis from which medical scientists can predict whether it will be possible to complete a 3-year flight. Now the crew is going through a readaptation period. During this period, 2 weeks after reentry, while still in the prophylactic clinic, the cosmonauts gave one of their first interviews to our correspondent. The interview is followed by commentary from medical specialists.

Question: You knew [ahead of time] that your flight would last a year; and were prepared for it. But as human beings were you homesick for Earth?

V. Titov: Well, even on Earth -- on a business trip, for example, you get homesick. And up there even more so! And in the final analysis this was a business trip too. An official one. And thus you do what you have been sent to do. We had no intention of returning earlier than scheduled .

Question: And how were your daily lives arranged on board? Didn't you, for example, get the urge to go to the baths, or to have a beer?

V. Titov: That's a good question! Actually we did have a bath on the station, although different from those on Earth, but as for beer.....

M. Manarov: ...We are healthy red-blooded [literally, living] men! In the words of our space Aesculapius -- he remained in orbit with the new crew -- since we are in the heavens, we must live like saints; however, nothing human is alien to us...

Question: Doctor Polyakov, it seems, treats not only the body, but the soul. But wasn't he the one who was so enthusiastic about some new kind of massage?

V. Titov: He brought this enthusiasm into space as well! And he helped us a great deal, especially after we took off our suits after EVAs. After all, we had been working for several hours under rather a lot of stress. And the doctor administered microrehabilitation after our exertion. In my case, for example, my back began to hurt and he got the pain to go away in two days by electric acupuncture, combined with ordinary and nerve-point massage..

Question: Tell me about EVAs.. What is it like to be suspended there above the abyss?

M. Manarov: How does it feel, do you mean? It feels as if you have ventured out into a boundless space -- the cosmos, which appears exactly the way it looked before the flight. It is true, though, that there were some things that surprised me. Who would have imagined that for some time after you have gone out into space, a "wind" continues to blow from the open airlock -- the remaining air is escaping, and freezing, and ice crystals are flying around! That I hadn't expected. As for the "surrounding landscape" -- it is all familiar from our observations through the window. And we were taught how to move around outside the ship while we were being trained on Earth.

Question: But you were outside the station for a long time. The station passed into the shadow of the Earth three and even four times, and yet you continued to work...

M. Manarov: In the dark, in principle, nothing changes. Lamps shine from "behind your ears," from the sides of your helmet. Only at the instant when night changes to day, do you suddenly lose your orientation for a minute: at first you can't figure out where you are in space, and in order to find your way, you have to look around.

Question: Do you orient yourself with respect to the station?

M. Manarov: Yes, on the basis of its design -- which we know well. but it is hard to see, you have to pay close attention if you want to know which way to go

Question: But while you are in the shadow, you can't see the Earth, can you?

M. Manarov: Actually you can -- where the Earth would be there is a gap with no stars. And if there's a moon, then the Earth can be seen clearly.

Question: And then you return to the station. How does it feel to spend day after day in a crowded enclosed space? Don't you have the sensation of being in some kind of alien, inhospitable world?

M.Manarov: Well, the cabins of the station are not all that small -- more than 100 cubic meters. And you have virtually everything you need to live and work.

V. Titov: And you get used to life up there relatively quickly. After 3 or 4 months everything around you grows habitual and familiar, sometimes you forget that you are in space. All your movements and shifting from one place to another seem natural, and are not troublesome at all. In the morning you get up, wash, shave, have breakfast, and go to work -- just like on Earth.

Question: Is Tsiolkovskiy's vision coming true and do people who live in weightlessness gradually turn into some kind of cosmic beings?

M. Manarov: Not yet. Although much is rapidly assimilated -- human beings have an enormous capacity to adapt. By the way, the other cosmonauts told us that "space" habits are retained on Earth. For example, you calmly let some object drop, confident that it will not fall, but float. I myself have not noticed this. All my reactions, feelings, and actions are purely terrestrial. Although in the plane returning to Moscow I noticed an interesting phenomenon. When you pick up some object which you didn't use in space -- for example, a cup of tea or coffee (since liquid does not flow in space, we use special utensils for drinking) then it seems completely normal, the way things ought to be. But when you pick up your watch -- mine went into space with me -- or your boots (we wore them on the station) then they seem very heavy. You pick up a boot by the lace, and it just weighs you down! It is five times heavier.. Evidently this is a kind of muscle memory.

Question: But don't you get the urge to fly the way you did in weightlessness.

M. Manarov: No. What is natural in one milieu is unnatural in another -- that is very firmly entrenched. But up there you have a great urge to walk! And for that reason we are very happy to use the "treadmill."

Question: Everyone is interested in how two individuals, each with his own habits, can live side by side for so long. One recalls the terrible tales of Jack London.

V. Titov: If you remember that crews are selected in accordance with the recommendations of psychologists, after long interviews, examinations, and discussions, this problem, I think, becomes considerably less difficult. We had no problem of incompatibility. Both cosmonauts had clear goals and internal motivation to fulfill our mission. In addition, one has to be easy going and not obnoxious.

Question: To the unenlightened mind, it would seem that such a long journey under unfamiliar conditions would have to have a psychological effect.

M. Manarov: I also thought about that during the years I was being prepared for flight. Somewhere in my subconscious there was the image of a small craft in an infinite void. And yet during the flight I never felt an emotion like fear. It simply did not occur. However, once in my sleep I suddenly saw myself in a small thin-walled capsule, flying somewhere into that same boundless void. Evidently that dream was an expression of my "subconscious feeling" so to speak. But when you are in the station -- it feels like a completely natural state: you work, you relax, you listen to the radio, you look out the window -- its hellishly beautiful out there. You feel no discomfort. Everything is normal.

Question: But after all, ahead of time, before the flight, it is no easy matter to guarantee the behavior of a person in all its details, 100 percent? Obviously neither he himself nor the physicians can do this, isn't that true?

M. Manarov: Today, having had more than a quarter century's experience in cosmonaut selection and training the physicians actually can predict and prevent, although not 100 percent. And that is why they turn gray on Earth during our flights..

V. Titov: As everyone knows, the body develops some kind of antibodies against poisons and has other physiological defense mechanisms. Perhaps something similar happens in psychology, in responses to various work situations. Perhaps these are also a kind of defense mechanism that permits a human being always, in spite of everything, to remain a human being. Perhaps, this is what helped me.

Question: In your case, Vladimir Georgiyevich, things were even more complicated. We were fans of yours. We remembered that you were pursued by misfortune: 5 years ago there was a problem with docking and you had to return to Earth. Then 6 months later there was a fire during launch. Then the crew was replaced and again you couldn't fly. How did you manage to overcome all this, keep up your will power, and prepare for a year's flight and complete it successfully?

V. Titov: To my mind there was nothing to overcome or keep up. There was only a feeling of dissatisfaction; that something in my life had not been completed, not experienced, not seen. Now, using hindsight, it is difficult to remember and analyze everything, but it seems to me everything went along in the usual way, normally. That's what failures are for, to give you the chance to test yourself again. Undoubtedly, this is the unconscious readiness for all eventualities, that is characteristic of many people.

Question: And now, you are again on Earth. How is the readaptation going?

M. Manarov: We went through a period I would call a time of surprise. At first I felt better than I could have imagined. Substantially better. And now, 2 weeks later, I am surprised that I am still not what I was before my flight. For example, by evening I am tired, I feel heavy.

V. Titov: When I walk I don't feel that there is anything wrong. In general, there are no disturbances; no vestibular shifts, or illusions. But when I try to run I clearly feel it: my legs are made of wood, my body is wooden. Everything has stabilized a hundred percent, but in the gym when I move too abruptly, I suddenly feel that something is not right.. But it can't be compared with the first moment after landing when I started to take off my suit in the search van and sat down and without noticing at all, suddenly began to fall over to the side, I noticed only when someone held me up! Weightlessness is a serious matter and still relatively poorly understood.

Question: More than 200 people have been in space, but you have had the longest experience of it. From the standpoint of this experience, what can you say about the flight to Mars?

M. Manarov: It is now clear: even a year-long flight requires much effort to prepare for properly, to allow cosmonauts to perform at a high level inflight, and return in a normal state. And what does this say about a 3-year flight? I think that problems arise with the selection of candidates. These must be people who are ready for anything. After all, the flight will be more than merely more complex and longer. The cosmonauts will spend the majority of the time in a closed environment; and Earth will not be right there nearby, instead there will be only empty space. This is a very important factor: when you can constantly see our beautiful planet shining in front of you, on which you can see rivers, seas, mountains, roads. You study them, you observe, sunsets and sunrises, you admire, you know that quite near you there are people living, the whole world! In other words there are many positive emotions enhancing the flight. Things will not be the same on the flight to Mars. But at the same time we already know that man adapts well, that he is capable of a great deal.

V. Titov. But such a flight, of course, will take place, probably, some time at the end of our century. We have technological capabilities to permit us to build the spacecraft necessary, of that there is no doubt. In duration the flight to Mars is closer to today's flight, than are those 108 minutes which Yuriy Gagarin spent in space. Thus, it is a matter of psychological preparation with a mindset for 3 years. And physiological preparation and reactions remain an open question. And let the medical people study all the data -- including ours -- and give their "OK." The main thing is that everything must be done logically, methodically, and carefully. We are optimists. We believe that man can think of everything and do everything that he has thought of.

The Physicians Comment

Evgeniy Kobzev, Crew Physician. The efforts of both the physicians and the crew were directed at solving two problems, to foresee every contingency in order to enable the crew to live for a whole year in space without any sort of illness, and to return to Earth in good condition. It is my opinion that both sides did their jobs successfully. The evidence for this is the results of readaptation: the cosmonauts felt well and objective parameters confirmed this.

Il'ya Tarasov, Chief Physician of the Cosmonaut Training Center. Who can foresee whether or not he will get sick during a given year? And yet we still had to prepare the cosmonauts physically, take therapeutic and prophylactic measures, and increase their functional capacities in order to minimize the probability of illness. As you can see, medicine was completely successful in doing this. The cosmonauts showed good endurance of acceleration and of the acute period of adaptation to weightlessness; they completed the strenuous, stressful flight program in an outstanding fashion, and after reentry left the spacecraft on their own two feet. All this was seen on television. Likewise, they left the aircraft and van under their own steam. And this after a whole year of weightlessness.

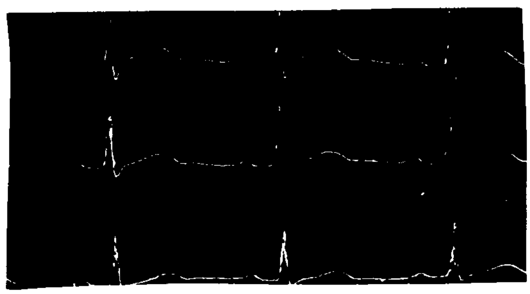
This was the result of the program scrupulously developed by the physicians and no less scrupulously followed by the cosmonauts, which constituted a kind of "health maintenance technology," including their daily schedule, various exercises, etc. But the effect of weightlessness is nonetheless great, and cannot be ignored. Take for example the system responsible for walking and standing erect. None of us can control it, it works by itself. But a sentry can stand at his post for 2 hours, while cosmonauts cannot do so after a flight. And during those first few minutes, although, of course, they did walk by themselves, they were wearing a special support suit and specially laced trousers, which helped them to maintain orthostatic tolerance, as we call it, or, to put it simply, to stand and walk upright. Of course, everything will recover, but it takes time, it requires readaptation.

The profession of cosmonaut is obviously the most difficult one in the world -- we, physicians, know that full well. Now, having developed a set of devices and means to maintain health and work capacity on board a spacecraft on a long-term flight, we can state with confidence that now people are able to fly to Mars. However, preparation for such a flight will require a great deal of effort on the part of the medical personnel.

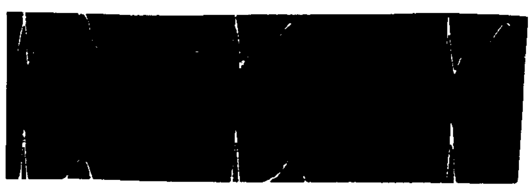
Anatoliy Zhernakov, Head of the Clinical Division. Much has been written in the press about technical, flight, and scientific training of the cosmonauts, and a great deal less about biomedical training. And yet the latter is of the greatest importance. The flight of this crew is an excellent confirmation of this. Take, for example, the following psychological fact: knowing that V. Titov, had met three times with various obstacles preventing him from entering orbit, we nevertheless entrusted him with this complex and prolonged flight. We knew very well who we were sending. His psychological and physical capacities enabled both us and him to make this decision. And we were right. And yet if we had not had faith in him this might, in a psychological sense, have "broken" him and he would have lost his faith in himself. It must be said that this conflict itself and its resolution and V. Titov's outstanding performance in flight -- all this is a major contribution to space medicine and psychology, essential for even longer flights.

This is the Way V. Titov's Electrocardiogram Changed

Preflight. Normal cardiogram



Postflight. It is obvious how the shape of the waves changed, suggesting certain changes in the elementary processes in the cardiac muscle (repolarization).



Four days postflight. Electrocardiogram has virtually normalized.

NASA National Aeronautics and Space Administration

Report Documentation Page

1. Report No.	2. Government Accession No.	3. Recipient's Catalog No.
NASA CR-3922(26)		

4. Title and Subtitle USSR Space Life Sciences Digest - Issue 22	5. Report Date August 1989
	6. Performing Organization Code
7. Author(s) Lydia Razran Hooke, Ronald Teeter, P. Lynn Donaldson, Victoria Garshnek,* and Joseph Rowe** (Editors)	8. Performing Organization Report No.
	10. Work Unit No.
9. Performing Organization Name and Address Lockheed Engineering and Sciences Company 600 Maryland Avenue, S.W. - Suite 600 Washington, DC 20024	11. Contract or Grant No. NASW-4292
	13. Type of Report and Period Covered Contractor Report
12. Sponsoring Agency Name and Address Office of Space Science and Applications National Aeronautics and Space Administration Washington, DC 20546	14. Sponsoring Agency Code EBM

15. Supplementary Notes

*GeorgeWashington University
**Library of Congress

16. Abstract

This is the twenty-second issue of NASA's USSR Space Life Sciences Digest. It contains abstracts of 56 journal papers or book chapters published in Russian and of a Soviet monograph reviewing the literature on chronobiology. The complete contents of two issues of the Soviet Journal *Space Biology and Aerospace Medicine* are covered. Selected abstracts are illustrated with figures and tables from the original. A special feature presents a translation of an interview with two Mir cosmonauts. The abstracts in this issue have been identified as relevant to 29 areas of space biology and medicine. These areas are: adaptation, biological rhythms, biospherics, body fluids, botany, cardiovascular and respiratory systems, developmental biology, endocrinology, enzymology, equipment and instrumentation, genetics, gravitational biology, habitability and environmental effects, hematology, human performance, immunology, life support systems, mathematical modeling, metabolism, microbiology, musculoskeletal system, neurophysiology, nutrition, operational medicine, perception, psychology, radiobiology, reproductive system, and space biology and medicine.

17. Key Words (Suggested by Author(s))	18. Distribution Statement
space life sciences, aerospace medicine, space biology,flight experiments, flight simulations, psychology and human performance, USSR, Soviet research	Unclassified - Unlimited Subject category 51

19. Security Classif. (of this report)	20. Security Classif. (of this page)	21. No. of pages	22. Price
Unclassified	Unlimited	140	A07

NASA FORM 1626 OCT 86

For sale by the National Technical Information Service, Springfield, Virginia 22161

NASA-Langley, 1989